* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2		"Ask CAS" for self-help around the clock
NEWS 3	JAN 27	Source of Registration (SR) information in REGISTRY updated and searchable
NEWS 4	JAN 27	A new search aid, the Company Name Thesaurus, available in CA/CAplus
NEWS 5	FEB 05	German (DE) application and patent publication number format changes
NEWS 6	MAR 03	MEDLINE and LMEDLINE reloaded
NEWS 7	MAR 03	MEDLINE file segment of TOXCENTER reloaded
NEWS 8	MAR 03	FRANCEPAT now available on STN
NEWS 9	MAR 29	Pharmaceutical Substances (PS) now available on STN
NEWS 10	MAR 29	WPIFV now available on STN
NEWS 11	MAR 29	No connect hour charges in WPIFV until May 1, 2004
NEWS 12	MAR 29	New monthly current-awareness alert (SDI) frequency in RAPRA
NEWS 13	APR 26	PROMT: New display field available
NEWS 14	APR 26	IFIPAT/IFIUDB/IFICDB: New super search and display field available
NEWS 15	APR 26	LITALERT now available on STN
NEWS 16	APR 27	NLDB: New search and display fields available

NEWS EXPRESS	MARCH 31 CURRENT WINDOWS VERSION IS V7.00A, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 26 APRIL 2004
NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS INTER	General Internet Information
NEWS LOGIN	Welcome Banner and News Items
NEWS PHONE	Direct Dial and Telecommunication Network Access to STN
NEWS WWW	CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that specific topic.

All use of STN is subject to the provisions of the STN Customer agreement. Please note that this agreement limits use to scientific research. Use for software development or design or implementation of commercial gateways or other similar uses is prohibited and may result in loss of user privileges and other penalties.

* * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 17:27:34 ON 07 MAY 2004

=> **file hcaplus**

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'HCAPLUS' ENTERED AT 17:27:42 ON 07 MAY 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 7 May 2004 VOL 140 ISS 20
FILE LAST UPDATED: 6 May 2004 (20040506/ED)

This file contains CAS Registry Numbers for easy and accurate
substance identification.

```
=> s somatostatin () receptor?
         17668 SOMATOSTATIN
           137 SOMATOSTATINS
         17676 SOMATOSTATIN
                 (SOMATOSTATIN OR SOMATOSTATINS)
        659894 RECEPTOR?
L1        2507 SOMATOSTATIN (W) RECEPTOR?

=> s l1 and regulat?
        821663 REGULAT?
L2         614 L1 AND REGULAT?

=> s l2 and pepti? () compound?
        427270 PEPTI?
        866680 COMPOUND?
       1007054 COMPD
       1558466 COMPDS
       2204442 COMPD
                 (COMPD OR COMPDS)
       2590835 COMPOUND?
                 (COMPOUND? OR COMPD)
          3142 PEPTI? (W) COMPOUND?
L3           1 L2 AND PEPTI? (W) COMPOUND?

=> d l3, ibib abs fhitstr, 1

L3   ANSWER 1 OF 1  HCAPLUS  COPYRIGHT 2004 ACS on STN
```

Full Text | Citing References

ACCESSION NUMBER: 1994:49086 HCAPLUS
DOCUMENT NUMBER: 120:49086
TITLE: Method using gamma-emitting radionuclide-labeled **peptide compd.** for intraoperatively detecting and locating tumor tissues, and therapeutic use
INVENTOR(S): Ensing, Geert Jacob; Panek, Karel Jan; Doedens, Bareld Jan
PATENT ASSIGNEE(S): Mallinckrodt Medical, Inc., USA
SOURCE: PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9318797	A1	19930930	WO 1993-US2772	19930324

```
        W:  AU, CA, JP, US
        RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
     AU 9339675         A1   19931021       AU 1993-39675     19930324
     EP 636032          A1   19950201       EP 1993-909165    19930324
        R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, NL, PT, SE
     JP 07505621        T2   19950622       JP 1993-516829    19930324
PRIORITY APPLN. INFO.:                     EP 1992-200848    19920325
                                           WO 1993-US2772    19930324
OTHER SOURCE(S):          MARPAT 120:49086
AB   A method of intraoperatively detecting an locating tumor tissues in the
     body of a warm-blooded living being comprises (1) parenterally
     administering a compn. of a peptide compd. (Markush included) labeled
     with a low-energy γ photon-emitting radionuclide, in a quantity
     sufficient for detection by a γ-detecting probe; (2) after the
     active substance is taken up by the tumor tissue and after blood clearance
     of radioactivity, using a radioimmunodetection technique in the relevant
     area of the body, using a γ-detecting probe.  The peptide may have
     neurokinin-1 receptor affinity or somatostatin receptor affinity or
     may be a cytokine, growth factor or hormone or deriv. or analog thereof.
     A method of radioguided surgery is also disclosed.  Combined use of the
     prepns. of the invention for detection and therapy is described.  Prepn.
     of a DTPA-octreotide kit and labeling of the DTPA-octreotide with e.g.
     Tb-161 is described.

=> d his

     (FILE 'HOME' ENTERED AT 17:27:34 ON 07 MAY 2004)

     FILE 'HCAPLUS' ENTERED AT 17:27:42 ON 07 MAY 2004
L1          2507 S SOMATOSTATIN () RECEPTOR?
L2           614 S L1 AND REGULAT?
L3             1 S L2 AND PEPTI? () COMPOUND?

=> s l2 and pepti?
         427270 PEPTI?
L4          224 L2 AND PEPTI?

=> s l2 and peptide?
         397078 PEPTIDE?
L5           219 L2 AND PEPTIDE?

=> s l5 and review/dt
        1723637 REVIEW/DT
L6           27 L5 AND REVIEW/DT

=> s l6 and duplicate remove
           8781 DUPLICATE
           1423 DUPLICATES
           9978 DUPLICATE
                (DUPLICATE OR DUPLICATES)
         170851 REMOVE
          28565 REMOVES
         196936 REMOVE
                (REMOVE OR REMOVES)
              0 DUPLICATE REMOVE
                (DUPLICATE(W)REMOVE)
L7            0 L6 AND DUPLICATE REMOVE
```

=> d l6, ibib abs fhitstr, 1-27

L6 ANSWER 1 OF 27 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2003:670193 HCAPLUS
DOCUMENT NUMBER: 140:86856
TITLE: **Somatostatin receptor** agonists and antagonists
AUTHOR(S): Crider, A. Michael
CORPORATE SOURCE: School of Pharmacy, University of Louisiana at Monroe, Monroe, LA, 71209-0470, USA
SOURCE: Expert Opinion on Therapeutic Patents (2003), 13(9), 1427-1441
CODEN: EOTPEG; ISSN: 1354-3776
PUBLISHER: Ashley Publications Ltd.
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review. Somatostatin is a cyclic **peptide** that is widely distributed in the CNS, the periphery and in a variety of tumors. Two biol. active forms, somatotropin release-inhibiting factor (SRIF)-14 and SRIF-28, exert their effects through activation of five G-protein-coupled receptor subtypes (sst1 - sst5). These **peptides** act as neurotransmitters or hormones and inhibit the secretion of other **peptides**, such as insulin, growth hormone and glucagon. Metabolically stable **peptide** and structurally diverse non-**peptide** analogs have been developed as subtype-selective agonists and antagonists. The availability of these novel SRIF analogs will greatly facilitate our understanding of the function and role of specific SRIF receptors. SRIF analogs offer therapeutic potential in the **regulation** of hormone secretion, diseases of the CNS and periphery and in the treatment and diagnosis of various tumors. This review will focus on an overview of SRIF, new developments related to SRIF role and function and the discovery of novel **peptide** and non-**peptide** agonists and antagonists.

REFERENCE COUNT: 102 THERE ARE 102 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 2 OF 27 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2003:363475 HCAPLUS
DOCUMENT NUMBER: 139:82803
TITLE: Growth **regulatory** factors and signaling proteins in testicular germ cell tumors
AUTHOR(S): Devouassoux-Shisheboran, Mojgan; Mauduit, Claire; Tabone, Eric; Droz, Jean Pierre; Benahmed, Mohamed
CORPORATE SOURCE: INSERM 407, Faculte de Medecine Lyon Sud, Oullins, F-69921, Fr.
SOURCE: APMIS (2003), 111(1), 212-224
CODEN: APMSEL; ISSN: 0903-4641
PUBLISHER: Blackwell Munksgaard
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review. The mol. basis of testicular germ cell tumorigenesis are not well elucidated. Growth factors **regulate** cell growth, differentiation and apoptosis. Major families of growth factors are present in the male gonad from early fetal development to adult life. They are involved in germ cell proliferation and differentiation. Growth signaling pathways suffer deregulation in many human malignancies. Given the importance of growth signals in normal testicular development and their acquired

deregulation in most human cancers, growth factors and signaling mols. that have been implicated in the genesis of testicular germ cell tumors, are reviewed. We detected a somatic mutation of SMAD4 gene, responsible for loss of protein function in seminomas. This mutational inactivation may affect the activity of several members of TGFβ superfamily (TGFβ, activin, inhibin, BMP). VEGF expression has been shown to predict metastasis in seminomas. A significant assocn. of HST-1 expression, a member of fibroblast growth factors, with the nonseminomatous phenotype and with tumor stage has been described. In contrast, C-KIT is expressed by seminomas only, from the preinvasive stage. Despite intense expression in almost all seminomas, activating mutation of C-KIT gene is seldom reported. Recently, the first animal model of classical testicular seminoma has been identified in transgenic mouse overexpressing GDNF. RET (GDNF receptor) expression is demonstrated in human seminomas, and not in nonseminomatous tumors. However, the exact mol. alterations of GDNF/RET/GFRα1 complex in germ cell tumors are not known. Finally, beside growth factors, other signaling mols. such as **peptide** hormones may be involved in testicular carcinogenesis. We have demonstrated a specific pattern of **somatostatin receptors** expression in each type of testicular germ cell tumors, with a loss of sst3 and sst4 in seminomas and loss of sst4 and expression of sst1 in nonseminomas only. These data suggest an antiproliferative action of somatostatin in testicular cancers. In summary, many growth factors and signaling mols. seem to represent specific markers for different histol. types of germ cell tumors (seminomas vs. nonseminomas) and may play a role in the differentiation of germ cell tumors. Despite a complex signaling pathway involved in the physiol. functions of male gonad, little is known about the implication of this signaling network in testicular malignancies. From a practical stand-point, further studies on the role of growth factors in human germ cell tumors may offer a new therapeutical perspective with the development of specific pharmacol. signaling modulators that could be used as therapeutic agents.

REFERENCE COUNT: 97 THERE ARE 97 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 3 OF 27 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2002:679185 HCAPLUS
DOCUMENT NUMBER: 138:283428
TITLE: **Peptide** receptor imaging: advances in the diagnosis of pulmonary diseases
AUTHOR(S): Van de Wiele, Christophe; Signore, Alberto; Dierckx, Rudi Andre
CORPORATE SOURCE: Division of Nuclear Medicine, Ghent University Hospital, Ghent, Belg.
SOURCE: American Journal of Respiratory Medicine (2002), 1(3), 177-183
CODEN: AJRMAG; ISSN: 1175-6365
PUBLISHER: Adis International Ltd.
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review. Radiolabeled cell-surface **peptide** receptor-binding mols. are emerging as an important class of radiopharmaceuticals. Their binding to specific cell membrane receptors allows for noninvasive assessment of regional receptor proteomics in vivo. Information thus obtained can be used for diagnostic purposes and for predicting and monitoring response to treatment. This paradigm also applies to pulmonary diseases. In this review, available radiopharmaceuticals of great potential or already in

clin. use for imaging of lung cancer, lung inflammation and infection and pulmonary embolism are discussed. In lung cancer, **somatostatin receptor** imaging by means of technetium-99m (99mTc)-octreotide scintigraphy has proven useful for characterizing malignancy in solitary pulmonary nodules. Addnl., several radiopharmaceuticals targeting tyrosine-kinase, e.g. 99mTc labeled epidermal growth factor and indium-111 (111In)-dicthylene triamine penta-acetic acid-trastuzumab, or G-protein coupled receptors, e.g. 99mTc-bombesin, iodine-123-vasoactive intestinal **peptide** and 111In-tetraazacyclododecane tetra-acetic acid (DOTA)-cholecystokinine-B, are being explored for their diagnostic as well as treatment monitoring potential. With the purpose of better evaluating the source of pulmonary embolism, as well as to differentiate acute from chronic deep venous thrombosis, several radiolabeled **peptides** targeting the glycoprotein IIb/IIIa fibrinogen receptor found on activated platelets have been developed. Out of these, 99mTc-P280 is now approved by the US Food and Drug Administration for scintigraphic imaging of suspected acute venous thrombosis in the lower extremities of patients. In the field of lung inflammation and infection, non-specific 111In and 99mTc-human polyclonal Igs have been successfully used to identify the presence and extent of Pneumocystis carinii, cytomegalovirus, Mycobaterium avium and fungal infections in patients with HIV infection. The clin. role of other radiopharmaceuticals such as 99mTc-J001X, a nonpyrogenic acylated polygalactoside isolated from Klebsiella pneumoniae and binding with high affinity to CD11b and CD14 lipopolysaccharide receptors expressed on monocytes/macrophages, and 111In-octreotide, binding to up-**regulated somatostatin receptors** on activated lymphocytes needs to be further defined.

REFERENCE COUNT: 62 THERE ARE 62 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 4 OF 27 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2002:622906 HCAPLUS
DOCUMENT NUMBER: 137:306652
TITLE: Diagnostic and therapeutic applications of radiolabeled somatostatin analogs: current status in an oncology center
AUTHOR(S): Podoloff, Donald A.
CORPORATE SOURCE: Nuclear Medicine, Texas Medical Center, Houston, TX, 77030-4095, USA
SOURCE: Current Pharmaceutical Design (2002), 8(20), 1809-1814
CODEN: CPDEFP; ISSN: 1381-6128
PUBLISHER: Bentham Science Publishers
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review. From the prospective of a major oncol. center in the United States, somatostatin analog radiopeptides currently have limited diagnostic and therapeutic utility. Diagnostic modalities utilizing **Somatostatin Receptor** Imaging are now com. available and the role of this type of method is currently being evaluated. Unlike the unique properties of thyroid tissue facilitating I-131 uptake, targeting of other tissues has required a carrier for the nuclide. Somastostatin **peptide** analogs have proved attractive based on the ubiquity of distribution and up-**regulation** in diseased tissue but prospective data is currently scarce. Interest in therapeutic applications of somatostatin analogs as carriers of yttrium, indium and more recently rhenium have resulted in trials with these agents both for endocrine and non-endocrine tumors. At this time, insufficient data exists to justify the indication of "first-line" therapy. The principles of **Somatostatin Receptor** Imaging

and radiotherapy are discussed in this article along with the current status of these modalities in clin. practice as viewed by the author.
REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 5 OF 27 HCAPLUS COPYRIGHT 2004 ACS on STN
Full Text | Citing References

ACCESSION NUMBER: 2002:549901 HCAPLUS
DOCUMENT NUMBER: 137:226726
TITLE: **Somatostatin receptor** subtypes: targeting functional and therapeutic specificity
AUTHOR(S): Culler, M.-D.; Taylor, J.-E.; Moreau, J.-P.
CORPORATE SOURCE: Biomeasure, incorporated/Beaufour - Ipsen Group, Milford, MA, 01757, USA
SOURCE: Annales d'Endocrinologie (2002), 63(2, Cah. 3), 2S5-2S12
CODEN: ANENAG; ISSN: 0003-4266
PUBLISHER: Masson Editeur
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: French
AB A review. Somatostatin is a **regulatory peptide** involved in a wide variety of biol. functions throughout the body. A key physiol. question, as well as the challenge to developing somatostatin-based therapeutics, is how functional specificity can be conferred in such a widespread, multifunctional hormonal system. With the discovery of distinct subtypes of the **somatostatin receptor**, we have attempted to elucidate the manner in which somatostatin selectively **regulates** specific biol. functions using panels of somatostatin analogs that have been fully characterized for their unique selectivity and specificity for the various receptor subtypes. By testing these selective analogs in well-established biol. assay systems, we and our collaborators have revealed functional interactions between the **somatostatin receptor** subtypes that can either potentiate or antagonize the cellular response to somatostatin. These observations have resulted in several novel concepts for treating acromegaly that should offer greater efficacy to a larger percentage of patients than current therapeutic options. Further, these studies are providing evidence of interaction between the **somatostatin receptor** subtypes and receptors of other G-protein-coupled receptor families. These various levels of interaction provide a means by which the cellular response to somatostatin can be exquisitely controlled and modified by both physiol. status and disease. Greater understanding of these interactions will provide the conceptual basis for future therapeutics with enhanced efficacy and with greater cellular and functional specificity.
REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 6 OF 27 HCAPLUS COPYRIGHT 2004 ACS on STN
Full Text | Citing References

ACCESSION NUMBER: 2001:439606 HCAPLUS
DOCUMENT NUMBER: 135:58639
TITLE: Somatostatins and their receptors in fish
AUTHOR(S): Lin, X.; Peter, R. E.
CORPORATE SOURCE: Department of Biological Sciences, University of Alberta, Edmonton, AB, T6G 2E9, Can.
SOURCE: Comparative Biochemistry and Physiology, Part B: Biochemistry & Molecular Biology (2001), 129B(2-3), 543-550

CODEN: CBPBB8; ISSN: 1096-4959
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review, with 62 refs. Somatostatin (SRIF) is a multigene family of **peptides**. SRIF-14 is conserved with identical primary structure in species across the vertebrates. The presence of multiple SRIF genes has been demonstrated in a no. of fish species. Notably, 3 distinct SRIF genes have been identified in goldfish. One of these genes, which encodes [Pro2]SRIF-14, has also been identified in sturgeon and African lungfish, and is closely assocd. with the amphibian [Pro2,Met13]SRIF-14 gene and mammalian cortistatin gene. The main neuroendocrine role of SRIF-14 **peptide** that has been detd. in fish is the inhibition of pituitary growth hormone secretion. The functions of SRIF-14 variant or larger forms of SRIF **peptide** and the **regulation** of SRIF gene expression remain to be explored. Type I and II SRIF receptors have been identified from goldfish and type III SRIF receptor from an elec. fish. Fish SRIF receptors display considerable homol. to mammalian counterparts in terms of primary structure and neg. coupling to adenylate cyclase. The identification of the multiple gene family of SRIF **peptides** and multiple types of SRIF receptors in fish opens a new avenue for the study of physiol. roles of SRIF, and the mol. and cellular mechanisms of SRIF actions in fish.

REFERENCE COUNT: 62 THERE ARE 62 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 7 OF 27 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2001:367623 HCAPLUS
DOCUMENT NUMBER: 135:103826
TITLE: From the biopolymer PHB to biological investigations of unnatural β- and γ-**peptides**
AUTHOR(S): Seebach, Dieter; Albert, Matthias; Arvidsson, Per I.; Rueping, Magnus; Schreiber, Jurg V.
CORPORATE SOURCE: Laboratorium fur Organische Chemie der Eidgenossischen Technischen Hochschule ETH Zentrum, Zurich, CH-8092, Switz.
SOURCE: Chimia (2001), 55(4), 345-353
CODEN: CHIMAD; ISSN: 0009-4293
PUBLISHER: Neue Schweizerische Chemische Gesellschaft
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review, with 62 refs. An overview is given of the past and present activities of the authors' group in the field of chem. biol. Thus, the polymer of 3-hydroxybutanoic acid (PHB), which is omnipresent in living organisms, triggered the authors' search for a better anal. for detecting PHB and the authors' syntheses of oligomers of 3-hydroxyalkanoic acids (OHBs). Also, the **regulation** of DNA replication by poly(β-malic acid) (PMA) in certain eukaryotes inspired synthetic work on the corresponding cyclic and open-chain oligomers. With these oligomers the authors not only tested the mechanisms of depolymerases, but were able to study the properties and activities of well-characterized compds. (also with isotope and fluorescence labeling). The role of PHB as component of ion transport systems through phospholipid bilayers was unambiguously established, and models for the channel structure were proposed. Replacement of amino acids by 3-hydroxybutanoic acid residues in **peptides** and replacement of the chain-bound oxygens in OHB by NH paved the authors' way into the world of β- and γ-**peptides**, the

synthesis and physiol. and pharmacol. properties of which are being investigated. β-**Peptides** are stable to peptidases, have a long lifetime in mammalian serum and are rather resistant to environmental microbial degrdn. The **peptides** consisting of homologated (β) or doubly homologated (γ) amino acids form stable secondary structures in soln. (helixes, turns, sheets) which can be used as scaffolds for **peptide** mimics, such as a β-tetrapeptide with affinity to a **somatostatin receptor** or a β-nonapeptide that inhibits intestinal lipid-transport protein (SR-Bl) in Caco-2 cells. Certain β-**peptides** have antibacterial, antiproliferative and hemolytic properties. The lessons from studies of β- and γ-**peptides** teach the authors about the central role of natural α-peptidic proteins.

REFERENCE COUNT: 62 THERE ARE 62 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 8 OF 27 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2001:24229 HCAPLUS
DOCUMENT NUMBER: 134:110586
TITLE: **Peptides** as **regulators** of the immune system: emphasis on somatostatin
AUTHOR(S): Krantic, S.
CORPORATE SOURCE: Faculte de Medecine Lyon-Sud, INSERM 407, Oullins, 69921, Fr.
SOURCE: Peptides (New York) (2000), 21(12), 1941-1964
CODEN: PPTDD5; ISSN: 0196-9781
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review with 165 refs. Study of the communication between nervous and immune systems culminated in the understanding that cytokines, formerly considered exclusively as immune system-derived **peptides**, are endogenous to the brain and display central actions. More recently, immune cells have been recognized as a peripheral source of "brain-specific" **peptides** with immunomodulatory actions. This article reviews studies concerning reciprocal effects of selected cytokines and neuropeptides in the nervous and immune systems, resp. The functional equivalence of these two categories of communicators is discussed with ref. to the example of the actions of neuropeptide somatostatin in the immune system.

REFERENCE COUNT: 165 THERE ARE 165 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 9 OF 27 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2001:20636 HCAPLUS
DOCUMENT NUMBER: 134:160374
TITLE: Somatostatin family of **peptides** and its receptors in fish
AUTHOR(S): Lin, Xinwei; Otto, Carla J.; Cardenas, Rodolfo; Peter, Richard E.
CORPORATE SOURCE: Department of Biological Sciences, University of Alberta, Edmonton, AB, T6G 2E9, Can.
SOURCE: Canadian Journal of Physiology and Pharmacology (2000), 78(12), 1053-1066
CODEN: CJPPA3; ISSN: 0008-4212

PUBLISHER: National Research Council of Canada
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English
AB A review, with 126 refs. Somatostatin (SRIF or SS) is a phylogenetically ancient, multigene family of **peptides**. SRIF-14 is conserved with identical primary structure in species of all classes of vertebrates. The presence of multiple SRIF genes has been demonstrated in a no. of fish species and could extend to tetrapods. Three distinct SRIF genes have been identified in goldfish. One of these genes, which encodes [Pro2]SRIF-14, is also present in sturgeon and African lungfish, and is closely assocd. with amphibian [Pro2,Met13]SRIF-14 gene and mammalian cortistatin gene. The post-translational processing of SRIF precursors could result in multiple forms of mature SRIF **peptides**, with differential abundance and tissue- or cell type-specific patterns. The main neuroendocrine role of SRIF-14 **peptide** that has been detd. in fish is the inhibition of pituitary growth hormone secretion. The functions of SRIF-14 variant or larger forms of SRIF **peptide** and the **regulation** of SRIF gene expression remain to be explored. Type 1 and type 2 SRIF receptors have been identified from goldfish and a type 3 SRIF receptor has been identified from an elec. fish. Fish SRIF receptors display considerable homol. with mammalian counterparts in terms of primary structure and neg. coupling to adenylate cyclase. Although addnl. types of receptors remain to be detd., identification of the multiple gene family of SRIF **peptides** and multiple types of SRIF receptors opens a new avenue for the study of physiol. roles of SRIF, and the mol. and cellular mechanisms of SRIF action in fish.
REFERENCE COUNT: 126 THERE ARE 126 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 10 OF 27 HCAPLUS COPYRIGHT 2004 ACS on STN
Full Text | Citing References
ACCESSION NUMBER: 2001:1361 HCAPLUS
DOCUMENT NUMBER: 134:157627
TITLE: Identification and characterization of subtype selective **somatostatin receptor** agonists
AUTHOR(S): Rohrer, Susan P.; Schaeffer, James M.
CORPORATE SOURCE: Department of Endocrinology and Chemical Biology, Merck Research Laboratories, Rahway, NJ, 07065, USA
SOURCE: Journal of Physiology (Paris) (2000), 94(3-4), 211-215
CODEN: JHYSEM; ISSN: 0928-4257
PUBLISHER: Editions Scientifiques et Medicales Elsevier
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English
AB A review with 11 refs. High affinity, subtype selective non-**peptide** agonists of **somatostatin receptor** subtypes 1-5 were identified in combinatorial libraries constructed based on mol. modeling of known **peptide** agonists. Simultaneous traditional chem. synthesis yielded an addnl. series of somatostatin subtype-2 receptor (SSTR2) selective agonists. These compds. have been used to further define the physiol. functions of the individual **somatostatin receptor** subtypes. In vitro expts. demonstrated the role of the SSTR2 in inhibition of glucagon release from mouse pancreatic α-cells and the somatostatin subtype-5 receptor (SSTR5) as a mediator of insulin secretion from pancreatic β-cells. Both SSTR2 and SSTR5 **regulated** growth hormone release from the rat anterior pituitary gland. In vivo studies performed with SSTR2 receptor selective compds. demonstrated effective inhibition of pulsatile growth hormone release in rats. The SSTR2 selective compds. also lowered plasma glucose levels in normal and diabetic animal models.

The availability of high affinity, subtype selective non-**peptide** agonists for each of the **somatostatin receptors** provides a direct approach to defining their physiol. function both peripherally and in the central nervous system.

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 11 OF 27 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2001:1360 HCAPLUS
DOCUMENT NUMBER: 134:141853
TITLE: Signal transduction of **somatostatin receptors** negatively controlling cell proliferation
AUTHOR(S): Ferjoux, Geraldine; Bousquet, Corinne; Cordelier, Pierre; Benali, Naoual; Lopez, Frederic; Rochaix, Philippe; Buscail, Louis; Susini, Christiane
CORPORATE SOURCE: Inserm U 151, CHU Rangueil, IFR 31, Toulouse, 31403, Fr.
SOURCE: Journal of Physiology (Paris) (2000), 94(3-4), 205-210
CODEN: JHYSEM; ISSN: 0928-4257
PUBLISHER: Editions Scientifiques et Medicales Elsevier
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review with 52 refs. Somatostatin acts as an inhibitory **peptide** of various secretory and proliferative responses. Its effects are mediated by a family of G-protein-coupled receptors (sst1-5) that can couple to diverse signal transduction pathways such as inhibition of adenylate cyclase and guanylate cyclase, modulation of ionic conductance channels, and protein dephosphorylation. The five receptors bind the natural **peptide** with high affinity but only sst2, sst5 and sst3 bind the short synthetic analogs. Somatostatin neg. **regulates** the growth of various normal and tumor cells. This effect is mediated indirectly through inhibition of secretion of growth-promoting factors, angiogenesis and modulation of the immune system. Somatostatin can also act directly through sst receptors present on target cells. The five receptors are expressed in various normal and tumor cells, the expression of each receptor being receptor subtype and cell type specific. According to the receptor subtypes, distinct signal transduction pathways are involved in the antiproliferative action of somatostatin. Sst1, 4 and 5 modulate the MAP kinase pathway and induce G1 cell cycle arrest. Sst3 and sst2 promote apoptosis by p53-dependent and -independent mechanisms, resp.

REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 12 OF 27 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2000:743172 HCAPLUS
DOCUMENT NUMBER: 134:16235
TITLE: The somatostatin immunoregulatory circuit present at sites of chronic inflammation
AUTHOR(S): Weinstock, Joel V.; Elliott, David
CORPORATE SOURCE: Division of Gastroenterology-Hepatology, Department of Medicine, University of Iowa, Iowa City, IA, 52242, USA
SOURCE: European Journal of Endocrinology (2000), 143(Suppl. 1), S15-S19
CODEN: EJOEEP; ISSN: 0804-4643
PUBLISHER: BioScientifica

DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English
AB A review with 23 refs. Somatostatin is part of an immunoregulatory circuit that helps limit interferon-γ (IFNγ) prodn. at sites of chronic inflammation. In murine schistosomiasis, parasite eggs induce focal, chronic granulomatous inflammation in the liver and intestines. These granulomas produce somatostatin 1-14 and express **somatostatin receptor** subtype no. 2 (SSTR2), which is the exclusive **somatostatin receptor** present in this inflammation. Granuloma and splenic macrophages as well as macrophage cell lines make somatostatin. There appears to be no other inflammatory cell source of the **peptide**. Various inflammatory mediators induce this expression, whereas substance P inhibits somatostatin prodn. Somatostatin can suppress IFNγ secretion from T cells via interaction with the SSTR2 receptor expressed on these cells. Other cells within the granuloma also display SSTR2. The effect of somatostatin on these other cell types remains unknown. The thymus of normal mice has a complete somatostatin **regulatory** circuit. The thymic epithelial and dendritic cells make somatostatin. Like the granulomas of murine schistosomiasis, the thymus expresses only SSTR2. Somatostatin likely has an important role in thymic T cell education and selection.
REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 13 OF 27 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2000:555026 HCAPLUS
DOCUMENT NUMBER: 133:278945
TITLE: Structure-function relationships of the signaling system for the somatostatin **peptide** hormone family
AUTHOR(S): Sheridan, Mark A.; Kittilson, Jeffrey D.; Slagter, Barton J.
CORPORATE SOURCE: Department of Zoology and Regulatory Biosciences Center, North Dakota State University, Fargo, ND, 58105, USA
SOURCE: American Zoologist (2000), 40(2), 269-286
CODEN: AMZOAF; ISSN: 0003-1569
PUBLISHER: Society for Integrative and Comparative Biology
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English
AB A review, with 135 refs. Somatostatins are a diverse family of **peptide** hormones that **regulate** a vast array of biol. processes in vertebrates, including the modulation of growth, development, and metab. The multi-functional nature of the somatostatin family arises from an elaborate, multi-faceted signaling system consisting of somatostatin signaling mols., G-protein-coupled receptors, and cellular effector pathways. A striking aspect of this signaling system is the substantial diversity at every level. The signal mols. themselves display considerable structural heterogeneity. This mol. heterogeneity results from tissue-specific differential processing of a single large precursor protein (preprosomatostatin) as well as from the existence of multiple somatostatin genes, each giving rise to different precursors. In addn., numerous SS receptor subtypes have been characterized (5 in mammals), some of which exhibit preferential binding to 1 ligand form over another. Propagation of the signal results from linkage of the receptors via numerous types of G-proteins to several different cellular effector pathways, including adenylyl cyclase, various protein kinases, numerous ion channels, and phospholipase C/inositol-3-phosphate. Ultimately, a particular response in a given target cell may be detd. by structural

interactions between and among the various elements of the signaling system.

REFERENCE COUNT: 135 THERE ARE 135 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 14 OF 27 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2000:70001 HCAPLUS
DOCUMENT NUMBER: 132:217183
TITLE: Treatment of endocrine gastroenteropancreatic tumors with somatostatin analogues
AUTHOR(S): Fehmann, H.-C.; Wulbrand, U.; Arnold, R.
CORPORATE SOURCE: Philipps-University of Marburg, Marburg, 35033, Germany
SOURCE: Recent Results in Cancer Research (2000), 153(Peptides in Oncology III), 15-22
CODEN: RRCRBU; ISSN: 0080-0015
PUBLISHER: Springer-Verlag
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review with 34 refs. Somatostatin is a hormone that **regulates** the function of several exocrine and endocrine glands. The **peptide** mediates its actions via five different receptors. These proteins are expressed in a tissue-specific manner. **Somatostatin receptors** are also present in neuroendocrine gastroenteropancreatic tumors. Two long-acting somatostatin analogs, octreotide and lanreotide, are recognized by the receptor subtypes 2 and 5. Excessive hormone secretion in carcinoid syndrome can be controlled by these drugs. In addn., at least a subgroup of patients with carcinoid syndromes respond with delayed tumor growth during octreotide therapy. In the future, the availability of the **somatostatin receptor** cDNAs will allow the development of specific and even more potent receptor analogs.

REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 15 OF 27 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1999:513710 HCAPLUS
DOCUMENT NUMBER: 131:266384
TITLE: Development of **somatostatin receptor** subtype selective agonists through combinatorial chemistry
AUTHOR(S): Rohrer, Susan P.; Berk, Scott C.
CORPORATE SOURCE: Department of Endocrinology and Chemical Biology, Merck Research Laboratories, Rahway, NJ, 07065, USA
SOURCE: Current Opinion in Drug Discovery & Development (1999), 2(4), 293-303
CODEN: CODDFF; ISSN: 1367-6733
PUBLISHER: Current Drugs Ltd.
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review with 47 refs. Non-**peptide** agonists of each of the five **somatostatin receptors** were identified from a combinatorial mixt. library and three follow-up libraries. The initial library (20 x 20 x 79) was patterned after a lead structure which was identified by screening a set of mols. selected on the basis of mol. modeling of known **peptide** agonists of the somatostatin subtype-2 receptor (SSTR2). A second library with increased complexity (21 x 22 x 147) was designed around the same

lead structure. Third and fourth libraries of aryl-indole compds. were designed, based on information that had been obtained by screening the first two libraries in five **somatostatin receptor** ligand-binding assays. Actives were chosen based on potency and receptor subtype selectivity profiles. The identity of each subtype selective compd. present in active mixts. was detd. by an iterative deconvolution process using resins archived from each step of the original synthesis. The approach of complex mixt. screening was well validated with each of the five **somatostatin receptors**. The advantages of mixt. screening with respect to manpower requirements, reagent consumption, and time to identify an active pure compd. from a mixt. were well illustrated in the course of this work. The availability of these high affinity, subtype selective agonists for each of the **somatostatin receptors** provided a direct approach to defining their physiol. functions. In vitro expts. demonstrated the role of the somatostatin subtype-2 receptor (SSTR2) in inhibition of glucagon release from mouse pancreatic α-cells and the somatostatin subtype-5 receptor (SSTR5) as a mediator of insulin secretion from pancreatic β-cells. Both receptors **regulated** growth hormone release from the rat anterior pituitary gland.

REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 16 OF 27 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1999:487829 HCAPLUS
DOCUMENT NUMBER: 131:332136
TITLE: Somatostatin and Its Receptor Family
AUTHOR(S): Patel, Yogesh C.
CORPORATE SOURCE: Fraser Laboratories, Department of Medicine, Department of Neurology and Neurosurgery, Department of Pharmacology and Therapeutics, Royal Victoria Hospital, Montreal Neurological Institute, Montreal, QC, H3A 1A1, Can.
SOURCE: Frontiers in Neuroendocrinology (1999), 20(3), 157-198
CODEN: FNEDA7; ISSN: 0091-3022
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review, with 233 refs. Somatostatin (SST), a **regulatory peptide**, is produced by neuroendocrine, inflammatory, and immune cells in response to ions, nutrients, neuropeptides, neurotransmitters, thyroid and steroid hormones, growth factors, and cytokines. The **peptide** is released in large amts. from storage pools of secretory cells, or in small amts. from activated immune and inflammatory cells, and acts as an endogenous inhibitory **regulator** of the secretory and proliferative responses of target cells that are widely distributed in the brain and periphery. These actions are mediated by a family of seven transmembrane (TM) domain G-protein-coupled receptors that comprise five distinct subtypes (termed SSTR1-5) that are encoded by sep. genes segregated on different chromosomes. The five receptor subtypes bind the natural SST **peptides**, SST-14 and SST-28, with low nanomolar affinity. Short synthetic octapeptide and hexapeptide analogs bind well to only three of the subtypes, 2, 3, and 5. Selective nonpeptide agonists with nanomolar affinity have been developed for four of the subtypes (SSTR1, 2, 3, and 4) and putative **peptide** antagonists for SSTR2 and SSTR5 have been identified. The ligand binding domain for SST ligands is made up of residues in TMs III-VII with a potential contribution by the second extracellular loop. SSTRs are widely expressed in many tissues, frequently as multiple subtypes that coexist in the same cell. The five

receptors share common signaling pathways such as the inhibition of adenylyl cyclase, activation of phosphotyrosine phosphatase (PTP), and modulation of mitogen-activated protein kinase (MAPK) through G-protein-dependent mechanisms. Some of the subtypes are also coupled to inward rectifying K+ channels (SSTR2, 3, 4, 5), to voltage-dependent Ca2+ channels (SSTR1, 2), a Na+/H+ exchanger (SSTR1), AMPA/kainate glutamate channels (SSTR1, 2), phospholipase C (SSTR2, 5), and phospholipase A2 (SSTR4). SSTRs block cell secretion by inhibiting intracellular cAMP and Ca2+ and by a receptor-linked distal effect on exocytosis. Four of the receptors (SSTR1, 2, 4, and 5) induce cell cycle arrest via PTP-dependent modulation of MAPK, assocd. with induction of the retinoblastoma tumor suppressor protein and p21. In contrast, SSTR3 uniquely triggers PTP-dependent apoptosis accompanied by activation of p53 and the pro-apoptotic protein Bax. SSTR1, 2, 3, and 5 display acute desensitization of adenylyl cyclase coupling. Four of the subtypes (SSTR2, 3, 4, and 5) undergo rapid agonist-dependent endocytosis. SSTR1 fails to be internalized but is instead upregulated at the membrane in response to continued agonist exposure. Among the wide spectrum of SST effects, several biol. responses have been identified that display abs. or relative subtype selectivity. These include GH secretion (SSTR2 and 5), insulin secretion (SSTR5), glucagon secretion (SSTR2), and immune responses (SSTR2). (c) 1999 Academic Press.

REFERENCE COUNT: 234 THERE ARE 234 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 17 OF 27 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1999:362864 HCAPLUS
DOCUMENT NUMBER: 131:139570
TITLE: Somatostatin as **regulator** of cardiovascular system activity
AUTHOR(S): Osadchiy, O. E.; Pokrovsky, V. M.
CORPORATE SOURCE: Kuban Medical Academy, Krasnodar, Russia
SOURCE: Uspekhi Fiziologicheskikh Nauk (1998), 29(4), 24-41
CODEN: UFZNAD; ISSN: 0301-1798
PUBLISHER: Nauka
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: Russian

AB A review with 146 refs. The control of cardiovascular system is provided not only by **regulatory** influence of classical neurotransmitters, acetylcholine and noradrenaline, but also some **regulatory peptides** have very important physiol. significance. One of them is somatostatin, a **peptide** which possess pronounced cardiotropic activity. Somatostatin-like immunoreactivity was found in the heart of several mammals including man; it was detected in the atrial and ventricular myocardium, conductive system of the heart and cardiac postganglionic parasympathetic neurons. Somatostatin co-exists with acetylcholine in presynaptic vagal endings and may be released by high-frequency stimulation of the vagus nerve. The main cardiac effects of somatostatin are heart rate deceleration, decrease of myocardial contractility and slowing of propagation velocity along conductive system of the heart. Somatostatin plays role in cardiac rhythmogenesis. It modifies electrophysiol. properties of cardiac pacemaker, modulates cardiac chronotropic action of autonomic nervous system and prevents supraventricular tachyarrhythmias. Somatostatin diminish cardiac output and affects blood pressure level; the character of vascular effects evoked by this **peptide** may be different in various species of animals. Somatostatin increases peripheral vascular resistance and provokes a

decrease of regional blood flow, esp. in mesenterial and hepatoportal vessels. This effect is great of clin. importance in case of gastroduodenal and esophageal bleedings. Cardiovascular effects of somatostatin may result from its modulatory action on presynaptic release of acetylcholine, noradrenaline and other humoral substances. Some effects of somatostatin result from its transmitter action which is provided by interaction of somatostatin with own receptors. **Somatostatin receptors** are coupled with adenylate cyclase activity and ion channels through inhibitory G-proteins. Excitation of **somatostatin receptors** causes a decrease of intracellular cAMP content, inhibition of inward calcium current and activation of potassium membrane conductance. There exist five different subtypes of **somatostatin receptors** which have different structure, pharmacol. properties and distribution in various tissues. The data presented in this review make it possible to conclude that cardiovascular effects of somatostatin are very important part in the spectrum of physiol. activity of this **peptide**.

L6 ANSWER 18 OF 27 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1999:214303 HCAPLUS
DOCUMENT NUMBER: 131:28027
TITLE: Somatostatin as a neurotrophic factor: which receptor/second messenger transduction system is involved?
AUTHOR(S): Schwartz, Joan P.; Zhang, Ji; Epelbaum, Jacques
CORPORATE SOURCE: Molecular Genetics Section, Clinical Neuroscience Branch, NINDS, NIH, Bethesda, MD, USA
SOURCE: Perspectives on Developmental Neurobiology (1998), 5(4), 427-435
CODEN: PDENED; ISSN: 1064-0517
PUBLISHER: Gordon & Breach Science Publishers
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review with 49 refs. A variety of studies support a trophic role for somatostatin in the developing nervous system, evidenced as stimulation of neurite outgrowth and axonal or neuronal migration in both in vivo and culture models. Cloning expts. have now demonstrated the existence of five subtypes of **somatostatin receptor**, differentially distributed in the nervous system, differentially linked to specific signal transduction systems and in certain cases differentially expressed during development. The combination of the differential and developmental **regulation** of expression of both the somatostatin **peptides** and their receptors thus provides great potential in terms of trophic effects. To substantiate trophic effects of somatostatin, data are presented from two different model systems, cultures of cerebellar granule cells as well as transgenic mice in which somatostatin is expressed under the control of the glial fibrillary acidic protein promoter. Finally, potential receptor subtypes and second messenger systems involved in these trophic effects are addressed.

REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 19 OF 27 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1998:304642 HCAPLUS
DOCUMENT NUMBER: 129:75837
TITLE: Lipopolysaccharide a virulence factor of Helicobacter pylori: effect of antiulcer agents

AUTHOR(S): Piotrowski, J.
CORPORATE SOURCE: Res. Center Univ. of Medicine and Dentistry of New Jersey, Newark, USA
SOURCE: Journal of Physiology and Pharmacology (1998), 49(1), 3-24
CODEN: JPHPEI; ISSN: 0867-5910
PUBLISHER: Polish Physiological Society
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review with 124 refs. Helicobacter pylori plays a major role in the pathogenesis of gastric disease. The gastric epithelial integrity is compromised by the H. pylori cell wall lipopolysaccharide untoward effect on the gastric epithelial cell receptors interaction with proteins of extracellular matrix, glycoproteins of mucus coat, and bioactive **peptides**. These interactions cause the weakening of the mucus coat rendering the underlying epithelium vulnerable to noxious luminal contents and the disrupting the **regulatory** feedback of somatostatin and gastrin. Moreover, H. pylori lipopolysaccharide induces histol. lesions typical of acute gastritis and these changes are reflected in the increased epithelial cell apoptosis. These findings thus identify cell wall lipopolysaccharide as a virulent factor responsible for the H. pylori effect on gastric epithelium. The effect of antiulcer agents on the interference of lipopolysaccharide with the laminin receptor was found to be most efficiently countered by ebrotidine, glycotide and sucralfate, whereas glycotide is the most potent in the reversal of the inhibitory effect of the lipopolysaccharide on mucin receptor binding. In the case of **somatostatin-receptor** binding, sucralfate followed by sucralfate and ebrotidine showed the most potency in of reversing the effect of H. pylori lipopolysaccharide. Thus these antiulcer agents have a great promise in the treatment gastric diseases assocd. with H. pylori infection.

REFERENCE COUNT: 105 THERE ARE 105 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 20 OF 27 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1997:316474 HCAPLUS
DOCUMENT NUMBER: 126:338919
TITLE: Neural monitoring system for circulating somatostatin in the hepatoportal area
AUTHOR(S): Nakabayashi, Hajime
CORPORATE SOURCE: Department of Internal Medicine, Graduate School of Medicine, Kanazawa University, Ishikawa, 920, Japan
SOURCE: Nutrition (Tarrytown, New York) (1997), 13(3), 225-229
CODEN: NUTRER; ISSN: 0899-9007
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review, with 17 refs. If a **peptide** hormone secreted from the gastroenteropancreatic (GEP) system is monitored by the hepatic vagal nerve, the nerve can signal the central nervous system and thereby exert control on its target organs. In this review, we offer a line of evidence for the hypothesis. When a physiol. dose of somatostatin (SS), one of the GEP hormones, was injected into the rat portal vein, the spike discharge rate in the hepatic afferent vagus increased significantly. This SS-induced activation of the vagus was completely abolished by a prior administration of our monoclonal antibody to SS receptor into the portal vein. We further disclosed a morphol. basis for this neural reception to

SS in the hepatoportal area: the neural bodies, located beneath the endothelium of the rat portal vein, preferentially bound the exogenous SS injected intraportally as revealed immunohistol. The bodies contained a structure of the nerve fiber arborizations resembling those of the afferent app. of Krause, on which the presence of SS receptor was confirmed histochem. using the anti-SS receptor antibody. These results provide a new insight into the receptor-mediated neural reception to GEP hormones in the hepatoportal area, implying the potential role of the reception GEP physiol.

REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 21 OF 27 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1997:222976 HCAPLUS
DOCUMENT NUMBER: 126:249511
TITLE: Relevance of **somatostatin receptors** and other **peptide** receptors in pathology
AUTHOR(S): Reubi, Jean Claude
CORPORATE SOURCE: Division of Cell Biology and Experimental Cancer Research, Institute of Pathology, University of Berne, Bern, CH-3010, Switz.
SOURCE: Endocrine Pathology (1997), 8(1), 11-20
CODEN: ENPAFD; ISSN: 1046-3976
PUBLISHER: Humana
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review, with 29 refs. Receptors for **regulatory peptides** can be overexpressed by several diseases, in particular by neoplasms. This review summarizes the current status of knowledge in this field, on the basis of in vitro receptor studies and with emphasis on receptors for somatostatin as well as for substance P (SP), VIP, and cholecystokinin. It evaluates the existing and potential clin. implications of the findings for diagnosis and therapy and discusses the role of the pathologist in this context.

L6 ANSWER 22 OF 27 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1997:81759 HCAPLUS
DOCUMENT NUMBER: 126:126978
TITLE: Molecular biology of **peptide** receptors
AUTHOR(S): Liapakis, G.; Reisine, T.
CORPORATE SOURCE: Department of Pharmacology, University of Pennsylvania School of Medicine, Philadelphia, PA, 19104, USA
SOURCE: Peptidergic Neuron, [International Symposium on Neurosecretion] 12th, Kiel, Sept. 20-22, 1995 (1996), Meeting Date 1995, 121-134. Editor(s): Krisch, Brigitte; Mentlein, Rolf. Birkhaeuser: Basel, Switz.
CODEN: 63XVA3
DOCUMENT TYPE: Conference; **General Review**
LANGUAGE: English

AB A review with approx. 60 refs. **Peptides** are a large class of endogenous mols. involved in neurotransmission. Most **peptide** receptors have a typical seven transmembrane spanning-like structure. Structure-function anal. of cloned **peptide** receptors has revealed important information on the ligand binding domains and regions of the receptors in coupling to G proteins and cellular effector systems. **Somatostatin receptors** consist of a family of five receptor subtypes which have approx. 50% amino

acid sequence identity. Selective ligands have been identified at 3 of the 5 receptors and have been useful in revealing distinct functions of those subtypes. The subtype SSTR2 mediates important physiol. actions of somatostatin including **regulation** of growth hormone release and is a target of anticancer agents. Ligand binding domains of this receptor have been identified using site-directed mutagenesis approaches. A region of four amino acids at the juncture of the third extracellular loop and transmembrane seven is involved in binding of synthetic hexa- and octapeptide analogs of somatostatin. A phenylalanine within this region is esp. crit. for binding octapeptide analogs such as Sandostatin. The third intracellular loop of this receptor may be particularly important in coupling the receptor to G proteins and appears to contain sites that may be involved in the desensitization of the receptor. In fact, this receptor becomes phosphorylated during desensitization. Phosphorylation of sites within the third intracellular loop of the receptor may be responsible for uncoupling the receptor from G proteins and cellular effector systems. Biochem. studies have revealed which G proteins assoc. with this receptor and have indicated that different G proteins link the receptor to distinct cellular effector systems. Because of the important physiol. roles of this receptor and its involvement in mediating therapeutic actions of somatostatin analogs, non-**peptide** SSTR2 drugs may have a no. of clin. uses. Structure-function anal. of this receptor may facilitate the development of these drugs.

L6 ANSWER 23 OF 27 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1996:482077 HCAPLUS
DOCUMENT NUMBER: 125:185921
TITLE: Molecular control of **peptide** hormone and receptor expression
AUTHOR(S): Dimaline, Rod
CORPORATE SOURCE: Physiological Laboratory, University Liverpool, Liverpool, L69 3BX, UK
SOURCE: Proceedings of the Nutrition Society (1996), 55(1B), 265-277
CODEN: PNUSA4; ISSN: 0029-6651
PUBLISHER: Cambridge University Press
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review, with 77 refs., on the 2 aspects of gastric endocrine cell gene expression: first, the rapid changes in gene expression that occur within a few min to a few h of ingestion of food or in response to changes in gastric lumen pH; and second, more slowly developing (days to weeks) adaptive changes that occur in response to chronic changes in the innervation of the stomach. The rapid changes were discussed in the context of the physiol. control of gastric acid secretion and the long-term changes were related to gastric mucosal protection. In addn., the expression and **regulation** of hormone receptors were discussed with ref. to somatostatin.

L6 ANSWER 24 OF 27 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1996:267409 HCAPLUS
DOCUMENT NUMBER: 124:312943
TITLE: Gastric secretion
AUTHOR(S): Schubert, Mitchell L.
CORPORATE SOURCE: Medical College of Virginia, Richmond, VA, USA
SOURCE: Current Opinion in Gastroenterology (1995), 11(6),

469-78
CODEN: COGAEK; ISSN: 0267-1379
PUBLISHER: Rapid Science Publishers
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English
AB A review, with 106 refs. This review of the past year's literature focuses on progress in the elucidation of the pathways and mechanisms controlling gastric exocrine (ie, acid and pepsin) and endocrine (ie, gastrin, histamine, and somatostatin) secretion at central, peripheral, and intracellular levels by neural, hormonal, and paracrine agents. Mol. biol. and immunocytochem. techniques coupled with physiol. studies have furthered the authors' understanding of the pathways and mechanisms **regulating** gastric secretions. At least three subtypes of muscarinic receptors, five subtypes of **somatostatin receptors**, and three subtypes of gastrin receptors have been identified, several of which participate in the **regulation** of acid secretion. γ-Aminobutyric acid has been identified convincingly in antral gastrin cells and tentatively in somatostatin-contg. D and serotonin-contg. enterochromaffin cells. Strong evidence supports the role of cholecystokinin and secretin as physiol. enterogastrones. Traditionally considered hormones, these **peptides** may inhibit acid secretion predominantly via vagal afferent nerve fibers. Cytoskeletal and low mol. mass GTP-binding proteins may participate in the **regulation** of membrane trafficking in parietal and chief cells.

L6 ANSWER 25 OF 27 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1991:670714 HCAPLUS
DOCUMENT NUMBER: 115:270714
TITLE: Cellular receptors implicated in epithelial transport
AUTHOR(S): Ruszniewski, P.
CORPORATE SOURCE: Serv. Gastroenterol., Hop. Bichat, Paris, F-75877, Fr.
SOURCE: Gastroenterologie Clinique et Biologique (1990), 14(12 bis), 29D-31D
CODEN: GCBIDC; ISSN: 0399-8320
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: French
AB A review, with 9 refs., of the role of **peptide** hormone receptors in intestinal epithelium transport. Specific topics discussed were expression of receptors during differentiation, gastrin and cholecystokinin receptors in gastric mucous membrane, receptors for **peptides** of the enteroglucagon family, and **somatostatin receptors**.

L6 ANSWER 26 OF 27 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1986:491447 HCAPLUS
DOCUMENT NUMBER: 105:91447
TITLE: **Regulation** of pancreatic acinar receptors by **peptides**
AUTHOR(S): Moessner, Joachim; Fischbach, Wolfgang
CORPORATE SOURCE: Med. Poliklin., Julius-Maximilians-Univ., Wuerzburg, D-8700, Fed. Rep. Ger.
SOURCE: Klinische Wochenschrift (1986), 64(11), 489-98
CODEN: KLWOAZ; ISSN: 0023-2173
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: German
AB A review, with 63 refs., on the **regulation** of pancreatic acinar receptors by **peptides**. The **peptides** may act on the same receptor they **regulate** or on other receptors causing **regulation** via receptor interactions. E.g., cholecystokinin causes desensitization of its own

receptor but also affects the **somatostatin receptor** capacity and affinity, the internalization of insulin-like growth factor and EGF receptors, and insulin receptor/cholecytokinin receptor interactions.

L6 ANSWER 27 OF 27 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1981:96391 HCAPLUS
DOCUMENT NUMBER: 94:96391
TITLE: **Regulation** of **peptide** receptors by homologous and heterologous ligands in cultured pituitary cells
AUTHOR(S): Schonbrunn, Agnes; Tashjian, Armen H., Jr.
CORPORATE SOURCE: Lab. Toxicol., Harvard Sch. Public Health, Boston, MA, 02115, USA
SOURCE: Endocrinol. Proc. Int. Congr. Endocrinol., 6th (1980), 579-82. Editor(s): Cumming, Ian A.; Funder, John W.; Mendelsohn, Frederick A. O. Elsevier/N. Holland Biomed. Press: Amsterdam, Neth.
CODEN: 44YLAV
DOCUMENT TYPE: Conference; **General Review**
LANGUAGE: English
AB A review with 12 refs. on the **regulation** of TRH [24305-27-9], somatostatin [51110-01-1], and epidermal growth factor [62229-50-9] receptors by homologous ligand of heterologous **peptides** in cultured somatotrophs.

=>

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2		"Ask CAS" for self-help around the clock
NEWS 3	JAN 27	Source of Registration (SR) information in REGISTRY updated and searchable
NEWS 4	JAN 27	A new search aid, the Company Name Thesaurus, available in CA/CAplus
NEWS 5	FEB 05	German (DE) application and patent publication number format changes
NEWS 6	MAR 03	MEDLINE and LMEDLINE reloaded
NEWS 7	MAR 03	MEDLINE file segment of TOXCENTER reloaded
NEWS 8	MAR 03	FRANCEPAT now available on STN
NEWS 9	MAR 29	Pharmaceutical Substances (PS) now available on STN
NEWS 10	MAR 29	WPIFV now available on STN
NEWS 11	MAR 29	No connect hour charges in WPIFV until May 1, 2004
NEWS 12	MAR 29	New monthly current-awareness alert (SDI) frequency in RAPRA
NEWS 13	APR 26	PROMT: New display field available
NEWS 14	APR 26	IFIPAT/IFIUDB/IFICDB: New super search and display field available
NEWS 15	APR 26	LITALERT now available on STN
NEWS 16	APR 27	NLDB: New search and display fields available

NEWS EXPRESS	MARCH 31 CURRENT WINDOWS VERSION IS V7.00A, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 26 APRIL 2004
NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS INTER	General Internet Information
NEWS LOGIN	Welcome Banner and News Items
NEWS PHONE	Direct Dial and Telecommunication Network Access to STN
NEWS WWW	CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that specific topic.

All use of STN is subject to the provisions of the STN Customer agreement. Please note that this agreement limits use to scientific research. Use for software development or design or implementation of commercial gateways or other similar uses is prohibited and may result in loss of user privileges and other penalties.

* * * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 17:27:34 ON 07 MAY 2004

=> **file hcaplus**

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'HCAPLUS' ENTERED AT 17:27:42 ON 07 MAY 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 7 May 2004 VOL 140 ISS 20
FILE LAST UPDATED: 6 May 2004 (20040506/ED)

This file contains CAS Registry Numbers for easy and accurate
substance identification.

```
=> s somatostatin () receptor?
         17668 SOMATOSTATIN
           137 SOMATOSTATINS
         17676 SOMATOSTATIN
                 (SOMATOSTATIN OR SOMATOSTATINS)
        659894 RECEPTOR?
L1        2507 SOMATOSTATIN (W) RECEPTOR?

=> s l1 and regulat?
        821663 REGULAT?
L2         614 L1 AND REGULAT?

=> s l2 and pepti? () compound?
        427270 PEPTI?
        866680 COMPOUND?
       1007054 COMPD
       1558466 COMPDS
       2204442 COMPD
                 (COMPD OR COMPDS)
       2590835 COMPOUND?
                 (COMPOUND? OR COMPD)
          3142 PEPTI? (W) COMPOUND?
L3           1 L2 AND PEPTI? (W) COMPOUND?

=> d l3, ibib abs fhitstr, 1

L3   ANSWER 1 OF 1  HCAPLUS  COPYRIGHT 2004 ACS on STN
```

Full Text | Citing References

ACCESSION NUMBER: 1994:49086 HCAPLUS
DOCUMENT NUMBER: 120:49086
TITLE: Method using gamma-emitting radionuclide-labeled **peptide compd.** for intraoperatively detecting and locating tumor tissues, and therapeutic use
INVENTOR(S): Ensing, Geert Jacob; Panek, Karel Jan; Doedens, Bareld Jan
PATENT ASSIGNEE(S): Mallinckrodt Medical, Inc., USA
SOURCE: PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9318797	A1	19930930	WO 1993-US2772	19930324

```
        W:  AU, CA, JP, US
        RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
     AU 9339675         A1   19931021       AU 1993-39675     19930324
     EP 636032          A1   19950201       EP 1993-909165    19930324
        R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, NL, PT, SE
     JP 07505621        T2   19950622       JP 1993-516829    19930324
PRIORITY APPLN. INFO.:                   EP 1992-200848      19920325
                                         WO 1993-US2772      19930324
OTHER SOURCE(S):         MARPAT 120:49086
AB   A method of intraoperatively detecting an locating tumor tissues in the
     body of a warm-blooded living being comprises (1) parenterally
     administering a compn. of a peptide compd. (Markush included) labeled
     with a low-energy γ photon-emitting radionuclide, in a quantity
     sufficient for detection by a γ-detecting probe; (2) after the
     active substance is taken up by the tumor tissue and after blood clearance
     of radioactivity, using a radioimmunodetection technique in the relevant
     area of the body, using a γ-detecting probe.  The peptide may have
     neurokinin-1 receptor affinity or somatostatin receptor affinity or
     may be a cytokine, growth factor or hormone or deriv. or analog thereof.
     A method of radioguided surgery is also disclosed.  Combined use of the
     prepns. of the invention for detection and therapy is described.  Prepn.
     of a DTPA-octreotide kit and labeling of the DTPA-octreotide with e.g.
     Tb-161 is described.


=> d his

     (FILE 'HOME' ENTERED AT 17:27:34 ON 07 MAY 2004)

     FILE 'HCAPLUS' ENTERED AT 17:27:42 ON 07 MAY 2004
L1          2507 S SOMATOSTATIN () RECEPTOR?
L2           614 S L1 AND REGULAT?
L3             1 S L2 AND PEPTI? () COMPOUND?

=> s l2 and pepti?
         427270 PEPTI?
L4          224 L2 AND PEPTI?

=> s l2 and peptide?
         397078 PEPTIDE?
L5          219 L2 AND PEPTIDE?

=> s l5 and review/dt
        1723637 REVIEW/DT
L6           27 L5 AND REVIEW/DT

=> s l6 and duplicate remove
           8781 DUPLICATE
           1423 DUPLICATES
           9978 DUPLICATE
                (DUPLICATE OR DUPLICATES)
         170851 REMOVE
          28565 REMOVES
         196936 REMOVE
                (REMOVE OR REMOVES)
              0 DUPLICATE REMOVE
                (DUPLICATE(W)REMOVE)
L7            0 L6 AND DUPLICATE REMOVE
```

=> d l6, ibib abs fhitstr, 1-27

L6 ANSWER 1 OF 27 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2003:670193 HCAPLUS
DOCUMENT NUMBER: 140:86856
TITLE: **Somatostatin receptor** agonists and antagonists
AUTHOR(S): Crider, A. Michael
CORPORATE SOURCE: School of Pharmacy, University of Louisiana at Monroe, Monroe, LA, 71209-0470, USA
SOURCE: Expert Opinion on Therapeutic Patents (2003), 13(9), 1427-1441
CODEN: EOTPEG; ISSN: 1354-3776
PUBLISHER: Ashley Publications Ltd.
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review. Somatostatin is a cyclic **peptide** that is widely distributed in the CNS, the periphery and in a variety of tumors. Two biol. active forms, somatotropin release-inhibiting factor (SRIF)-14 and SRIF-28, exert their effects through activation of five G-protein-coupled receptor subtypes (sst1 - sst5). These **peptides** act as neurotransmitters or hormones and inhibit the secretion of other **peptides**, such as insulin, growth hormone and glucagon. Metabolically stable **peptide** and structurally diverse non-**peptide** analogs have been developed as subtype-selective agonists and antagonists. The availability of these novel SRIF analogs will greatly facilitate our understanding of the function and role of specific SRIF receptors. SRIF analogs offer therapeutic potential in the **regulation** of hormone secretion, diseases of the CNS and periphery and in the treatment and diagnosis of various tumors. This review will focus on an overview of SRIF, new developments related to SRIF role and function and the discovery of novel **peptide** and non-**peptide** agonists and antagonists.

REFERENCE COUNT: 102 THERE ARE 102 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 2 OF 27 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2003:363475 HCAPLUS
DOCUMENT NUMBER: 139:82803
TITLE: Growth **regulatory** factors and signaling proteins in testicular germ cell tumors
AUTHOR(S): Devouassoux-Shisheboran, Mojgan; Mauduit, Claire; Tabone, Eric; Droz, Jean Pierre; Benahmed, Mohamed
CORPORATE SOURCE: INSERM 407, Faculte de Medecine Lyon Sud, Oullins, F-69921, Fr.
SOURCE: APMIS (2003), 111(1), 212-224
CODEN: APMSEL; ISSN: 0903-4641
PUBLISHER: Blackwell Munksgaard
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review. The mol. basis of testicular germ cell tumorigenesis are not well elucidated. Growth factors **regulate** cell growth, differentiation and apoptosis. Major families of growth factors are present in the male gonad from early fetal development to adult life. They are involved in germ cell proliferation and differentiation. Growth signaling pathways suffer deregulation in many human malignancies. Given the importance of growth signals in normal testicular development and their acquired

deregulation in most human cancers, growth factors and signaling mols. that have been implicated in the genesis of testicular germ cell tumors, are reviewed. We detected a somatic mutation of SMAD4 gene, responsible for loss of protein function in seminomas. This mutational inactivation may affect the activity of several members of TGFβ superfamily (TGFβ, activin, inhibin, BMP). VEGF expression has been shown to predict metastasis in seminomas. A significant assocn. of HST-1 expression, a member of fibroblast growth factors, with the nonseminomatous phenotype and with tumor stage has been described. In contrast, C-KIT is expressed by seminomas only, from the preinvasive stage. Despite intense expression in almost all seminomas, activating mutation of C-KIT gene is seldom reported. Recently, the first animal model of classical testicular seminoma has been identified in transgenic mouse overexpressing GDNF. RET (GDNF receptor) expression is demonstrated in human seminomas, and not in nonseminomatous tumors. However, the exact mol. alterations of GDNF/RET/GFRα1 complex in germ cell tumors are not known. Finally, beside growth factors, other signaling mols. such as **peptide** hormones may be involved in testicular carcinogenesis. We have demonstrated a specific pattern of **somatostatin receptors** expression in each type of testicular germ cell tumors, with a loss of sst3 and sst4 in seminomas and loss of sst4 and expression of sst1 in nonseminomas only. These data suggest an antiproliferative action of somatostatin in testicular cancers. In summary, many growth factors and signaling mols. seem to represent specific markers for different histol. types of germ cell tumors (seminomas vs. nonseminomas) and may play a role in the differentiation of germ cell tumors. Despite a complex signaling pathway involved in the physiol. functions of male gonad, little is known about the implication of this signaling network in testicular malignancies. From a practical stand-point, further studies on the role of growth factors in human germ cell tumors may offer a new therapeutical perspective with the development of specific pharmacol. signaling modulators that could be used as therapeutic agents.

REFERENCE COUNT: 97 THERE ARE 97 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 3 OF 27 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2002:679185 HCAPLUS
DOCUMENT NUMBER: 138:283428
TITLE: **Peptide** receptor imaging: advances in the diagnosis of pulmonary diseases
AUTHOR(S): Van de Wiele, Christophe; Signore, Alberto; Dierckx, Rudi Andre
CORPORATE SOURCE: Division of Nuclear Medicine, Ghent University Hospital, Ghent, Belg.
SOURCE: American Journal of Respiratory Medicine (2002), 1(3), 177-183
CODEN: AJRMAG; ISSN: 1175-6365
PUBLISHER: Adis International Ltd.
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review. Radiolabeled cell-surface **peptide** receptor-binding mols. are emerging as an important class of radiopharmaceuticals. Their binding to specific cell membrane receptors allows for noninvasive assessment of regional receptor proteomics in vivo. Information thus obtained can be used for diagnostic purposes and for predicting and monitoring response to treatment. This paradigm also applies to pulmonary diseases. In this review, available radiopharmaceuticals of great potential or already in

clin. use for imaging of lung cancer, lung inflammation and infection and pulmonary embolism are discussed. In lung cancer, **somatostatin receptor** imaging by means of technetium-99m (99mTc)-octreotide scintigraphy has proven useful for characterizing malignancy in solitary pulmonary nodules. Addnl., several radiopharmaceuticals targeting tyrosine-kinase, e.g. 99mTc labeled epidermal growth factor and indium-111 (111In)-dicthylene triamine penta-acetic acid-trastuzumab, or G-protein coupled receptors, e.g. 99mTc-bombesin, iodine-123-vasoactive intestinal **peptide** and 111In-tetraazacyclododecane tetra-acetic acid (DOTA)-cholecystokinine-B, are being explored for their diagnostic as well as treatment monitoring potential. With the purpose of better evaluating the source of pulmonary embolism, as well as to differentiate acute from chronic deep venous thrombosis, several radiolabeled **peptides** targeting the glycoprotein IIb/IIIa fibrinogen receptor found on activated platelets have been developed. Out of these, 99mTc-P280 is now approved by the US Food and Drug Administration for scintigraphic imaging of suspected acute venous thrombosis in the lower extremities of patients. In the field of lung inflammation and infection, non-specific 111In and 99mTc-human polyclonal Igs have been successfully used to identify the presence and extent of Pneumocystis carinii, cytomegalovirus, Mycobaterium avium and fungal infections in patients with HIV infection. The clin. role of other radiopharmaceuticals such as 99mTc-J001X, a nonpyrogenic acylated polygalactoside isolated from Klebsiella pneumoniae and binding with high affinity to CD11b and CD14 lipopolysaccharide receptors expressed on monocytes/macrophages, and 111In-octreotide, binding to up-**regulated somatostatin receptors** on activated lymphocytes needs to be further defined.

REFERENCE COUNT: 62 THERE ARE 62 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 4 OF 27 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2002:622906 HCAPLUS
DOCUMENT NUMBER: 137:306652
TITLE: Diagnostic and therapeutic applications of radiolabeled somatostatin analogs: current status in an oncology center
AUTHOR(S): Podoloff, Donald A.
CORPORATE SOURCE: Nuclear Medicine, Texas Medical Center, Houston, TX, 77030-4095, USA
SOURCE: Current Pharmaceutical Design (2002), 8(20), 1809-1814
CODEN: CPDEFP; ISSN: 1381-6128
PUBLISHER: Bentham Science Publishers
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review. From the prospective of a major oncol. center in the United States, somatostatin analog radiopeptides currently have limited diagnostic and therapeutic utility. Diagnostic modalities utilizing **Somatostatin Receptor** Imaging are now com. available and the role of this type of method is currently being evaluated. Unlike the unique properties of thyroid tissue facilitating I-131 uptake, targeting of other tissues has required a carrier for the nuclide. Somastostatin **peptide** analogs have proved attractive based on the ubiquity of distribution and up-**regulation** in diseased tissue but prospective data is currently scarce. Interest in therapeutic applications of somatostatin analogs as carriers of yttrium, indium and more recently rhenium have resulted in trials with these agents both for endocrine and non-endocrine tumors. At this time, insufficient data exists to justify the indication of "first-line" therapy. The principles of **Somatostatin Receptor** Imaging

and radiotherapy are discussed in this article along with the current status of these modalities in clin. practice as viewed by the author.
REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 5 OF 27 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2002:549901 HCAPLUS
DOCUMENT NUMBER: 137:226726
TITLE: **Somatostatin receptor** subtypes: targeting functional and therapeutic specificity
AUTHOR(S): Culler, M.-D.; Taylor, J.-E.; Moreau, J.-P.
CORPORATE SOURCE: Biomeasure, incorporated/Beaufour - Ipsen Group, Milford, MA, 01757, USA
SOURCE: Annales d'Endocrinologie (2002), 63(2, Cah. 3), 2S5-2S12
CODEN: ANENAG; ISSN: 0003-4266
PUBLISHER: Masson Editeur
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: French
AB A review. Somatostatin is a **regulatory peptide** involved in a wide variety of biol. functions throughout the body. A key physiol. question, as well as the challenge to developing somatostatin-based therapeutics, is how functional specificity can be conferred in such a widespread, multifunctional hormonal system. With the discovery of distinct subtypes of the **somatostatin receptor**, we have attempted to elucidate the manner in which somatostatin selectively **regulates** specific biol. functions using panels of somatostatin analogs that have been fully characterized for their unique selectivity and specificity for the various receptor subtypes. By testing these selective analogs in well-established biol. assay systems, we and our collaborators have revealed functional interactions between the **somatostatin receptor** subtypes that can either potentiate or antagonize the cellular response to somatostatin. These observations have resulted in several novel concepts for treating acromegaly that should offer greater efficacy to a larger percentage of patients than current therapeutic options. Further, these studies are providing evidence of interaction between the **somatostatin receptor** subtypes and receptors of other G-protein-coupled receptor families. These various levels of interaction provide a means by which the cellular response to somatostatin can be exquisitely controlled and modified by both physiol. status and disease. Greater understanding of these interactions will provide the conceptual basis for future therapeutics with enhanced efficacy and with greater cellular and functional specificity.
REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 6 OF 27 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2001:439606 HCAPLUS
DOCUMENT NUMBER: 135:58639
TITLE: Somatostatins and their receptors in fish
AUTHOR(S): Lin, X.; Peter, R. E.
CORPORATE SOURCE: Department of Biological Sciences, University of Alberta, Edmonton, AB, T6G 2E9, Can.
SOURCE: Comparative Biochemistry and Physiology, Part B: Biochemistry & Molecular Biology (2001), 129B(2-3), 543-550

CODEN: CBPBB8; ISSN: 1096-4959
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review, with 62 refs. Somatostatin (SRIF) is a multigene family of **peptides**. SRIF-14 is conserved with identical primary structure in species across the vertebrates. The presence of multiple SRIF genes has been demonstrated in a no. of fish species. Notably, 3 distinct SRIF genes have been identified in goldfish. One of these genes, which encodes [Pro2]SRIF-14, has also been identified in sturgeon and African lungfish, and is closely assocd. with the amphibian [Pro2,Met13]SRIF-14 gene and mammalian cortistatin gene. The main neuroendocrine role of SRIF-14 **peptide** that has been detd. in fish is the inhibition of pituitary growth hormone secretion. The functions of SRIF-14 variant or larger forms of SRIF **peptide** and the **regulation** of SRIF gene expression remain to be explored. Type I and II SRIF receptors have been identified from goldfish and type III SRIF receptor from an elec. fish. Fish SRIF receptors display considerable homol. to mammalian counterparts in terms of primary structure and neg. coupling to adenylate cyclase. The identification of the multiple gene family of SRIF **peptides** and multiple types of SRIF receptors in fish opens a new avenue for the study of physiol. roles of SRIF, and the mol. and cellular mechanisms of SRIF actions in fish.

REFERENCE COUNT: 62 THERE ARE 62 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 7 OF 27 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2001:367623 HCAPLUS
DOCUMENT NUMBER: 135:103826
TITLE: From the biopolymer PHB to biological investigations of unnatural β- and γ-**peptides**
AUTHOR(S): Seebach, Dieter; Albert, Matthias; Arvidsson, Per I.; Rueping, Magnus; Schreiber, Jurg V.
CORPORATE SOURCE: Laboratorium fur Organische Chemie der Eidgenossischen Technischen Hochschule ETH Zentrum, Zurich, CH-8092, Switz.
SOURCE: Chimia (2001), 55(4), 345-353
CODEN: CHIMAD; ISSN: 0009-4293
PUBLISHER: Neue Schweizerische Chemische Gesellschaft
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review, with 62 refs. An overview is given of the past and present activities of the authors' group in the field of chem. biol. Thus, the polymer of 3-hydroxybutanoic acid (PHB), which is omnipresent in living organisms, triggered the authors' search for a better anal. for detecting PHB and the authors' syntheses of oligomers of 3-hydroxyalkanoic acids (OHBs). Also, the **regulation** of DNA replication by poly(β-malic acid) (PMA) in certain eukaryotes inspired synthetic work on the corresponding cyclic and open-chain oligomers. With these oligomers the authors not only tested the mechanisms of depolymerases, but were able to study the properties and activities of well-characterized compds. (also with isotope and fluorescence labeling). The role of PHB as component of ion transport systems through phospholipid bilayers was unambiguously established, and models for the channel structure were proposed. Replacement of amino acids by 3-hydroxybutanoic acid residues in **peptides** and replacement of the chain-bound oxygens in OHB by NH paved the authors' way into the world of β- and γ-**peptides**, the

synthesis and physiol. and pharmacol. properties of which are being investigated. β-**Peptides** are stable to peptidases, have a long lifetime in mammalian serum and are rather resistant to environmental microbial degrdn. The **peptides** consisting of homologated (β) or doubly homologated (γ) amino acids form stable secondary structures in soln. (helixes, turns, sheets) which can be used as scaffolds for **peptide** mimics, such as a β-tetrapeptide with affinity to a **somatostatin receptor** or a β-nonapeptide that inhibits intestinal lipid-transport protein (SR-B1) in Caco-2 cells. Certain β-**peptides** have antibacterial, antiproliferative and hemolytic properties. The lessons from studies of β- and γ-**peptides** teach the authors about the central role of natural α-peptidic proteins.

REFERENCE COUNT: 62 THERE ARE 62 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 8 OF 27 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2001:24229 HCAPLUS
DOCUMENT NUMBER: 134:110586
TITLE: **Peptides** as **regulators** of the immune system: emphasis on somatostatin
AUTHOR(S): Krantic, S.
CORPORATE SOURCE: Faculte de Medecine Lyon-Sud, INSERM 407, Oullins, 69921, Fr.
SOURCE: Peptides (New York) (2000), 21(12), 1941-1964
CODEN: PPTDD5; ISSN: 0196-9781
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review with 165 refs. Study of the communication between nervous and immune systems culminated in the understanding that cytokines, formerly considered exclusively as immune system-derived **peptides**, are endogenous to the brain and display central actions. More recently, immune cells have been recognized as a peripheral source of "brain-specific" **peptides** with immunomodulatory actions. This article reviews studies concerning reciprocal effects of selected cytokines and neuropeptides in the nervous and immune systems, resp. The functional equivalence of these two categories of communicators is discussed with ref. to the example of the actions of neuropeptide somatostatin in the immune system.

REFERENCE COUNT: 165 THERE ARE 165 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 9 OF 27 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2001:20636 HCAPLUS
DOCUMENT NUMBER: 134:160374
TITLE: Somatostatin family of **peptides** and its receptors in fish
AUTHOR(S): Lin, Xinwei; Otto, Carla J.; Cardenas, Rodolfo; Peter, Richard E.
CORPORATE SOURCE: Department of Biological Sciences, University of Alberta, Edmonton, AB, T6G 2E9, Can.
SOURCE: Canadian Journal of Physiology and Pharmacology (2000), 78(12), 1053-1066
CODEN: CJPPA3; ISSN: 0008-4212

PUBLISHER: National Research Council of Canada
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English
AB A review, with 126 refs. Somatostatin (SRIF or SS) is a phylogenetically ancient, multigene family of **peptides**. SRIF-14 is conserved with identical primary structure in species of all classes of vertebrates. The presence of multiple SRIF genes has been demonstrated in a no. of fish species and could extend to tetrapods. Three distinct SRIF genes have been identified in goldfish. One of these genes, which encodes [Pro2]SRIF-14, is also present in sturgeon and African lungfish, and is closely assocd. with amphibian [Pro2,Met13]SRIF-14 gene and mammalian cortistatin gene. The post-translational processing of SRIF precursors could result in multiple forms of mature SRIF **peptides**, with differential abundance and tissue- or cell type-specific patterns. The main neuroendocrine role of SRIF-14 **peptide** that has been detd. in fish is the inhibition of pituitary growth hormone secretion. The functions of SRIF-14 variant or larger forms of SRIF **peptide** and the **regulation** of SRIF gene expression remain to be explored. Type 1 and type 2 SRIF receptors have been identified from goldfish and a type 3 SRIF receptor has been identified from an elec. fish. Fish SRIF receptors display considerable homol. with mammalian counterparts in terms of primary structure and neg. coupling to adenylate cyclase. Although addnl. types of receptors remain to be detd., identification of the multiple gene family of SRIF **peptides** and multiple types of SRIF receptors opens a new avenue for the study of physiol. roles of SRIF, and the mol. and cellular mechanisms of SRIF action in fish.
REFERENCE COUNT: 126 THERE ARE 126 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 10 OF 27 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2001:1361 HCAPLUS
DOCUMENT NUMBER: 134:157627
TITLE: Identification and characterization of subtype selective **somatostatin receptor** agonists
AUTHOR(S): Rohrer, Susan P.; Schaeffer, James M.
CORPORATE SOURCE: Department of Endocrinology and Chemical Biology, Merck Research Laboratories, Rahway, NJ, 07065, USA
SOURCE: Journal of Physiology (Paris) (2000), 94(3-4), 211-215
CODEN: JHYSEM; ISSN: 0928-4257
PUBLISHER: Editions Scientifiques et Medicales Elsevier
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English
AB A review with 11 refs. High affinity, subtype selective non-**peptide** agonists of **somatostatin receptor** subtypes 1-5 were identified in combinatorial libraries constructed based on mol. modeling of known **peptide** agonists. Simultaneous traditional chem. synthesis yielded an addnl. series of somatostatin subtype-2 receptor (SSTR2) selective agonists. These compds. have been used to further define the physiol. functions of the individual **somatostatin receptor** subtypes. In vitro expts. demonstrated the role of the SSTR2 in inhibition of glucagon release from mouse pancreatic α-cells and the somatostatin subtype-5 receptor (SSTR5) as a mediator of insulin secretion from pancreatic β-cells. Both SSTR2 and SSTR5 **regulated** growth hormone release from the rat anterior pituitary gland. In vivo studies performed with SSTR2 receptor selective compds. demonstrated effective inhibition of pulsatile growth hormone release in rats. The SSTR2 selective compds. also lowered plasma glucose levels in normal and diabetic animal models.

The availability of high affinity, subtype selective non-**peptide** agonists for each of the **somatostatin receptors** provides a direct approach to defining their physiol. function both peripherally and in the central nervous system.

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 11 OF 27 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2001:1360 HCAPLUS
DOCUMENT NUMBER: 134:141853
TITLE: Signal transduction of **somatostatin receptors** negatively controlling cell proliferation
AUTHOR(S): Ferjoux, Geraldine; Bousquet, Corinne; Cordelier, Pierre; Benali, Naoual; Lopez, Frederic; Rochaix, Philippe; Buscail, Louis; Susini, Christiane
CORPORATE SOURCE: Inserm U 151, CHU Rangueil, IFR 31, Toulouse, 31403, Fr.
SOURCE: Journal of Physiology (Paris) (2000), 94(3-4), 205-210
CODEN: JHYSEM; ISSN: 0928-4257
PUBLISHER: Editions Scientifiques et Medicales Elsevier
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review with 52 refs. Somatostatin acts as an inhibitory **peptide** of various secretory and proliferative responses. Its effects are mediated by a family of G-protein-coupled receptors (sst1-5) that can couple to diverse signal transduction pathways such as inhibition of adenylate cyclase and guanylate cyclase, modulation of ionic conductance channels, and protein dephosphorylation. The five receptors bind the natural **peptide** with high affinity but only sst2, sst5 and sst3 bind the short synthetic analogs. Somatostatin neg. **regulates** the growth of various normal and tumor cells. This effect is mediated indirectly through inhibition of secretion of growth-promoting factors, angiogenesis and modulation of the immune system. Somatostatin can also act directly through sst receptors present on target cells. The five receptors are expressed in various normal and tumor cells, the expression of each receptor being receptor subtype and cell type specific. According to the receptor subtypes, distinct signal transduction pathways are involved in the antiproliferative action of somatostatin. Sst1, 4 and 5 modulate the MAP kinase pathway and induce G1 cell cycle arrest. Sst3 and sst2 promote apoptosis by p53-dependent and -independent mechanisms, resp.

REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 12 OF 27 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2000:743172 HCAPLUS
DOCUMENT NUMBER: 134:16235
TITLE: The somatostatin immunoregulatory circuit present at sites of chronic inflammation
AUTHOR(S): Weinstock, Joel V.; Elliott, David
CORPORATE SOURCE: Division of Gastroenterology-Hepatology, Department of Medicine, University of Iowa, Iowa City, IA, 52242, USA
SOURCE: European Journal of Endocrinology (2000), 143(Suppl. 1), S15-S19
CODEN: EJOEEP; ISSN: 0804-4643
PUBLISHER: BioScientifica

DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English
AB A review with 23 refs. Somatostatin is part of an immunoregulatory circuit that helps limit interferon-γ (IFNγ) prodn. at sites of chronic inflammation. In murine schistosomiasis, parasite eggs induce focal, chronic granulomatous inflammation in the liver and intestines. These granulomas produce somatostatin 1-14 and express **somatostatin receptor** subtype no. 2 (SSTR2), which is the exclusive **somatostatin receptor** present in this inflammation. Granuloma and splenic macrophages as well as macrophage cell lines make somatostatin. There appears to be no other inflammatory cell source of the **peptide**. Various inflammatory mediators induce this expression, whereas substance P inhibits somatostatin prodn. Somatostatin can suppress IFNγ secretion from T cells via interaction with the SSTR2 receptor expressed on these cells. Other cells within the granuloma also display SSTR2. The effect of somatostatin on these other cell types remains unknown. The thymus of normal mice has a complete somatostatin **regulatory** circuit. The thymic epithelial and dendritic cells make somatostatin. Like the granulomas of murine schistosomiasis, the thymus expresses only SSTR2. Somatostatin likely has an important role in thymic T cell education and selection.
REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 13 OF 27 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2000:555026 HCAPLUS
DOCUMENT NUMBER: 133:278945
TITLE: Structure-function relationships of the signaling system for the somatostatin **peptide** hormone family
AUTHOR(S): Sheridan, Mark A.; Kittilson, Jeffrey D.; Slagter, Barton J.
CORPORATE SOURCE: Department of Zoology and Regulatory Biosciences Center, North Dakota State University, Fargo, ND, 58105, USA
SOURCE: American Zoologist (2000), 40(2), 269-286
CODEN: AMZOAF; ISSN: 0003-1569
PUBLISHER: Society for Integrative and Comparative Biology
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English
AB A review, with 135 refs. Somatostatins are a diverse family of **peptide** hormones that **regulate** a vast array of biol. processes in vertebrates, including the modulation of growth, development, and metab. The multi-functional nature of the somatostatin family arises from an elaborate, multi-faceted signaling system consisting of somatostatin signaling mols., G-protein-coupled receptors, and cellular effector pathways. A striking aspect of this signaling system is the substantial diversity at every level. The signal mols. themselves display considerable structural heterogeneity. This mol. heterogeneity results from tissue-specific differential processing of a single large precursor protein (preprosomatostatin) as well as from the existence of multiple somatostatin genes, each giving rise to different precursors. In addn., numerous SS receptor subtypes have been characterized (5 in mammals), some of which exhibit preferential binding to 1 ligand form over another. Propagation of the signal results from linkage of the receptors via numerous types of G-proteins to several different cellular effector pathways, including adenylyl cyclase, various protein kinases, numerous ion channels, and phospholipase C/inositol-3-phosphate. Ultimately, a particular response in a given target cell may be detd. by structural

interactions between and among the various elements of the signaling system.
REFERENCE COUNT: 135 THERE ARE 135 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 14 OF 27 HCAPLUS COPYRIGHT 2004 ACS on STN
Full Text | Citing References

ACCESSION NUMBER: 2000:70001 HCAPLUS
DOCUMENT NUMBER: 132:217183
TITLE: Treatment of endocrine gastroenteropancreatic tumors with somatostatin analogues
AUTHOR(S): Fehmann, H.-C.; Wulbrand, U.; Arnold, R.
CORPORATE SOURCE: Philipps-University of Marburg, Marburg, 35033, Germany
SOURCE: Recent Results in Cancer Research (2000), 153(Peptides in Oncology III), 15-22
CODEN: RRCRBU; ISSN: 0080-0015
PUBLISHER: Springer-Verlag
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English
AB A review with 34 refs. Somatostatin is a hormone that **regulates** the function of several exocrine and endocrine glands. The **peptide** mediates its actions via five different receptors. These proteins are expressed in a tissue-specific manner. **Somatostatin receptors** are also present in neuroendocrine gastroenteropancreatic tumors. Two long-acting somatostatin analogs, octreotide and lanreotide, are recognized by the receptor subtypes 2 and 5. Excessive hormone secretion in carcinoid syndrome can be controlled by these drugs. In addn., at least a subgroup of patients with carcinoid syndromes respond with delayed tumor growth during octreotide therapy. In the future, the availability of the **somatostatin receptor** cDNAs will allow the development of specific and even more potent receptor analogs.
REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 15 OF 27 HCAPLUS COPYRIGHT 2004 ACS on STN
Full Text | Citing References

ACCESSION NUMBER: 1999:513710 HCAPLUS
DOCUMENT NUMBER: 131:266384
TITLE: Development of **somatostatin receptor** subtype selective agonists through combinatorial chemistry
AUTHOR(S): Rohrer, Susan P.; Berk, Scott C.
CORPORATE SOURCE: Department of Endocrinology and Chemical Biology, Merck Research Laboratories, Rahway, NJ, 07065, USA
SOURCE: Current Opinion in Drug Discovery & Development (1999), 2(4), 293-303
CODEN: CODDFF; ISSN: 1367-6733
PUBLISHER: Current Drugs Ltd.
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English
AB A review with 47 refs. Non-**peptide** agonists of each of the five **somatostatin receptors** were identified from a combinatorial mixt. library and three follow-up libraries. The initial library (20 x 20 x 79) was patterned after a lead structure which was identified by screening a set of mols. selected on the basis of mol. modeling of known **peptide** agonists of the somatostatin subtype-2 receptor (SSTR2). A second library with increased complexity (21 x 22 x 147) was designed around the same

lead structure. Third and fourth libraries of aryl-indole compds. were designed, based on information that had been obtained by screening the first two libraries in five **somatostatin receptor** ligand-binding assays. Actives were chosen based on potency and receptor subtype selectivity profiles. The identity of each subtype selective compd. present in active mixts. was detd. by an iterative deconvolution process using resins archived from each step of the original synthesis. The approach of complex mixt. screening was well validated with each of the five **somatostatin receptors**. The advantages of mixt. screening with respect to manpower requirements, reagent consumption, and time to identify an active pure compd. from a mixt. were well illustrated in the course of this work. The availability of these high affinity, subtype selective agonists for each of the **somatostatin receptors** provided a direct approach to defining their physiol. functions. In vitro expts. demonstrated the role of the somatostatin subtype-2 receptor (SSTR2) in inhibition of glucagon release from mouse pancreatic α-cells and the somatostatin subtype-5 receptor (SSTR5) as a mediator of insulin secretion from pancreatic β-cells. Both receptors **regulated** growth hormone release from the rat anterior pituitary gland.

REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 16 OF 27 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1999:487829 HCAPLUS
DOCUMENT NUMBER: 131:332136
TITLE: Somatostatin and Its Receptor Family
AUTHOR(S): Patel, Yogesh C.
CORPORATE SOURCE: Fraser Laboratories, Department of Medicine, Department of Neurology and Neurosurgery, Department of Pharmacology and Therapeutics, Royal Victoria Hospital, Montreal Neurological Institute, Montreal, QC, H3A 1A1, Can.
SOURCE: Frontiers in Neuroendocrinology (1999), 20(3), 157-198
CODEN: FNEDA7; ISSN: 0091-3022
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review, with 233 refs. Somatostatin (SST), a **regulatory peptide**, is produced by neuroendocrine, inflammatory, and immune cells in response to ions, nutrients, neuropeptides, neurotransmitters, thyroid and steroid hormones, growth factors, and cytokines. The **peptide** is released in large amts. from storage pools of secretory cells, or in small amts. from activated immune and inflammatory cells, and acts as an endogenous inhibitory **regulator** of the secretory and proliferative responses of target cells that are widely distributed in the brain and periphery. These actions are mediated by a family of seven transmembrane (TM) domain G-protein-coupled receptors that comprise five distinct subtypes (termed SSTR1-5) that are encoded by sep. genes segregated on different chromosomes. The five receptor subtypes bind the natural SST **peptides**, SST-14 and SST-28, with low nanomolar affinity. Short synthetic octapeptide and hexapeptide analogs bind well to only three of the subtypes, 2, 3, and 5. Selective nonpeptide agonists with nanomolar affinity have been developed for four of the subtypes (SSTR1, 2, 3, and 4) and putative **peptide** antagonists for SSTR2 and SSTR5 have been identified. The ligand binding domain for SST ligands is made up of residues in TMs III-VII with a potential contribution by the second extracellular loop. SSTRs are widely expressed in many tissues, frequently as multiple subtypes that coexist in the same cell. The five

receptors share common signaling pathways such as the inhibition of adenylyl cyclase, activation of phosphotyrosine phosphatase (PTP), and modulation of mitogen-activated protein kinase (MAPK) through G-protein-dependent mechanisms. Some of the subtypes are also coupled to inward rectifying K+ channels (SSTR2, 3, 4, 5), to voltage-dependent Ca2+ channels (SSTR1, 2), a Na+/H+ exchanger (SSTR1), AMPA/kainate glutamate channels (SSTR1, 2), phospholipase C (SSTR2, 5), and phospholipase A2 (SSTR4). SSTRs block cell secretion by inhibiting intracellular cAMP and Ca2+ and by a receptor-linked distal effect on exocytosis. Four of the receptors (SSTR1, 2, 4, and 5) induce cell cycle arrest via PTP-dependent modulation of MAPK, assocd. with induction of the retinoblastoma tumor suppressor protein and p21. In contrast, SSTR3 uniquely triggers PTP-dependent apoptosis accompanied by activation of p53 and the pro-apoptotic protein Bax. SSTR1, 2, 3, and 5 display acute desensitization of adenylyl cyclase coupling. Four of the subtypes (SSTR2, 3, 4, and 5) undergo rapid agonist-dependent endocytosis. SSTR1 fails to be internalized but is instead upregulated at the membrane in response to continued agonist exposure. Among the wide spectrum of SST effects, several biol. responses have been identified that display abs. or relative subtype selectivity. These include GH secretion (SSTR2 and 5), insulin secretion (SSTR5), glucagon secretion (SSTR2), and immune responses (SSTR2). (c) 1999 Academic Press.

REFERENCE COUNT: 234 THERE ARE 234 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 17 OF 27 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1999:362864 HCAPLUS
DOCUMENT NUMBER: 131:139570
TITLE: Somatostatin as **regulator** of cardiovascular system activity
AUTHOR(S): Osadchiy, O. E.; Pokrovsky, V. M.
CORPORATE SOURCE: Kuban Medical Academy, Krasnodar, Russia
SOURCE: Uspekhi Fiziologicheskikh Nauk (1998), 29(4), 24-41
CODEN: UFZNAD; ISSN: 0301-1798
PUBLISHER: Nauka
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: Russian

AB A review with 146 refs. The control of cardiovascular system is provided not only by **regulatory** influence of classical neurotransmitters, acetylcholine and noradrenaline, but also some **regulatory peptides** have very important physiol. significance. One of them is somatostatin, a **peptide** which possess pronounced cardiotropic activity. Somatostatin-like immunoreactivity was found in the heart of several mammals including man; it was detected in the atrial and ventricular myocardium, conductive system of the heart and cardiac postganglionic parasympathetic neurons. Somatostatin co-exists with acetylcholine in presynaptic vagal endings and may be released by high-frequency stimulation of the vagus nerve. The main cardiac effects of somatostatin are heart rate deceleration, decrease of myocardial contractility and slowing of propagation velocity along conductive system of the heart. Somatostatin plays role in cardiac rhythmogenesis. It modifies electrophysiol. properties of cardiac pacemaker, modulates cardiac chronotropic action of autonomic nervous system and prevents supraventricular tachyarrhythmias. Somatostatin diminish cardiac output and affects blood pressure level; the character of vascular effects evoked by this **peptide** may be different in various species of animals. Somatostatin increases peripheral vascular resistance and provokes a

decrease of regional blood flow, esp. in mesenterial and hepatoportal vessels. This effect is great of clin. importance in case of gastroduodenal and esophageal bleedings. Cardiovascular effects of somatostatin may result from its modulatory action on presynaptic release of acetylcholine, noradrenaline and other humoral substances. Some effects of somatostatin result from its transmitter action which is provided by interaction of somatostatin with own receptors. **Somatostatin receptors** are coupled with adenylate cyclase activity and ion channels through inhibitory G-proteins. Excitation of **somatostatin receptors** causes a decrease of intracellular cAMP content, inhibition of inward calcium current and activation of potassium membrane conductance. There exist five different subtypes of **somatostatin receptors** which have different structure, pharmacol. properties and distribution in various tissues. The data presented in this review make it possible to conclude that cardiovascular effects of somatostatin are very important part in the spectrum of physiol. activity of this **peptide**.

L6 ANSWER 18 OF 27 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1999:214303 HCAPLUS
DOCUMENT NUMBER: 131:28027
TITLE: Somatostatin as a neurotrophic factor: which receptor/second messenger transduction system is involved?
AUTHOR(S): Schwartz, Joan P.; Zhang, Ji; Epelbaum, Jacques
CORPORATE SOURCE: Molecular Genetics Section, Clinical Neuroscience Branch, NINDS, NIH, Bethesda, MD, USA
SOURCE: Perspectives on Developmental Neurobiology (1998), 5(4), 427-435
CODEN: PDENED; ISSN: 1064-0517
PUBLISHER: Gordon & Breach Science Publishers
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review with 49 refs. A variety of studies support a trophic role for somatostatin in the developing nervous system, evidenced as stimulation of neurite outgrowth and axonal or neuronal migration in both in vivo and culture models. Cloning expts. have now demonstrated the existence of five subtypes of **somatostatin receptor**, differentially distributed in the nervous system, differentially linked to specific signal transduction systems and in certain cases differentially expressed during development. The combination of the differential and developmental **regulation** of expression of both the somatostatin **peptides** and their receptors thus provides great potential in terms of trophic effects. To substantiate trophic effects of somatostatin, data are presented from two different model systems, cultures of cerebellar granule cells as well as transgenic mice in which somatostatin is expressed under the control of the glial fibrillary acidic protein promoter. Finally, potential receptor subtypes and second messenger systems involved in these trophic effects are addressed.

REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 19 OF 27 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1998:304642 HCAPLUS
DOCUMENT NUMBER: 129:75837
TITLE: Lipopolysaccharide a virulence factor of Helicobacter pylori: effect of antiulcer agents

AUTHOR(S): Piotrowski, J.
CORPORATE SOURCE: Res. Center Univ. of Medicine and Dentistry of New Jersey, Newark, USA
SOURCE: Journal of Physiology and Pharmacology (1998), 49(1), 3-24
CODEN: JPHPEI; ISSN: 0867-5910
PUBLISHER: Polish Physiological Society
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review with 124 refs. Helicobacter pylori plays a major role in the pathogenesis of gastric disease. The gastric epithelial integrity is compromised by the H. pylori cell wall lipopolysaccharide untoward effect on the gastric epithelial cell receptors interaction with proteins of extracellular matrix, glycoproteins of mucus coat, and bioactive **peptides**. These interactions cause the weakening of the mucus coat rendering the underlying epithelium vulnerable to noxious luminal contents and the disrupting the **regulatory** feedback of somatostatin and gastrin. Moreover, H. pylori lipopolysaccharide induces histol. lesions typical of acute gastritis and these changes are reflected in the increased epithelial cell apoptosis. These findings thus identify cell wall lipopolysaccharide as a virulent factor responsible for the H. pylori effect on gastric epithelium. The effect of antiulcer agents on the interference of lipopolysaccharide with the laminin receptor was found to be most efficiently countered by ebrotidine, glycotide and sucralfate, whereas glycotide is the most potent in the reversal of the inhibitory effect of the lipopolysaccharide on mucin receptor binding. In the case of **somatostatin-receptor** binding, sucralfate followed by sucralfate and ebrotidine showed the most potency in of reversing the effect of H. pylori lipopolysaccharide. Thus these antiulcer agents have a great promise in the treatment gastric diseases assocd. with H. pylori infection.

REFERENCE COUNT: 105 THERE ARE 105 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 20 OF 27 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1997:316474 HCAPLUS
DOCUMENT NUMBER: 126:338919
TITLE: Neural monitoring system for circulating somatostatin in the hepatoportal area
AUTHOR(S): Nakabayashi, Hajime
CORPORATE SOURCE: Department of Internal Medicine, Graduate School of Medicine, Kanazawa University, Ishikawa, 920, Japan
SOURCE: Nutrition (Tarrytown, New York) (1997), 13(3), 225-229
CODEN: NUTRER; ISSN: 0899-9007
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review, with 17 refs. If a **peptide** hormone secreted from the gastroenteropancreatic (GEP) system is monitored by the hepatic vagal nerve, the nerve can signal the central nervous system and thereby exert control on its target organs. In this review, we offer a line of evidence for the hypothesis. When a physiol. dose of somatostatin (SS), one of the GEP hormones, was injected into the rat portal vein, the spike discharge rate in the hepatic afferent vagus increased significantly. This SS-induced activation of the vagus was completely abolished by a prior administration of our monoclonal antibody to SS receptor into the portal vein. We further disclosed a morphol. basis for this neural reception to

SS in the hepatoportal area: the neural bodies, located beneath the endothelium of the rat portal vein, preferentially bound the exogenous SS injected intraportally as revealed immunohistol. The bodies contained a structure of the nerve fiber arborizations resembling those of the afferent app. of Krause, on which the presence of SS receptor was confirmed histochem. using the anti-SS receptor antibody. These results provide a new insight into the receptor-mediated neural reception to GEP hormones in the hepatoportal area, implying the potential role of the reception GEP physiol.

REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 21 OF 27 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1997:222976 HCAPLUS
DOCUMENT NUMBER: 126:249511
TITLE: Relevance of **somatostatin receptors** and other **peptide** receptors in pathology
AUTHOR(S): Reubi, Jean Claude
CORPORATE SOURCE: Division of Cell Biology and Experimental Cancer Research, Institute of Pathology, University of Berne, Bern, CH-3010, Switz.
SOURCE: Endocrine Pathology (1997), 8(1), 11-20
CODEN: ENPAFD; ISSN: 1046-3976
PUBLISHER: Humana
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review, with 29 refs. Receptors for **regulatory peptides** can be overexpressed by several diseases, in particular by neoplasms. This review summarizes the current status of knowledge in this field, on the basis of in vitro receptor studies and with emphasis on receptors for somatostatin as well as for substance P (SP), VIP, and cholecystokinin. It evaluates the existing and potential clin. implications of the findings for diagnosis and therapy and discusses the role of the pathologist in this context.

L6 ANSWER 22 OF 27 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1997:81759 HCAPLUS
DOCUMENT NUMBER: 126:126978
TITLE: Molecular biology of **peptide** receptors
AUTHOR(S): Liapakis, G.; Reisine, T.
CORPORATE SOURCE: Department of Pharmacology, University of Pennsylvania School of Medicine, Philadelphia, PA, 19104, USA
SOURCE: Peptidergic Neuron, [International Symposium on Neurosecretion] 12th, Kiel, Sept. 20-22, 1995 (1996), Meeting Date 1995, 121-134. Editor(s): Krisch, Brigitte; Mentlein, Rolf. Birkhaeuser: Basel, Switz.
CODEN: 63XVA3
DOCUMENT TYPE: Conference; **General Review**
LANGUAGE: English

AB A review with approx. 60 refs. **Peptides** are a large class of endogenous mols. involved in neurotransmission. Most **peptide** receptors have a typical seven transmembrane spanning-like structure. Structure-function anal. of cloned **peptide** receptors has revealed important information on the ligand binding domains and regions of the receptors in coupling to G proteins and cellular effector systems. **Somatostatin receptors** consist of a family of five receptor subtypes which have approx. 50% amino

acid sequence identity. Selective ligands have been identified at 3 of the 5 receptors and have been useful in revealing distinct functions of those subtypes. The subtype SSTR2 mediates important physiol. actions of somatostatin including **regulation** of growth hormone release and is a target of anticancer agents. Ligand binding domains of this receptor have been identified using site-directed mutagenesis approaches. A region of four amino acids at the juncture of the third extracellular loop and transmembrane seven is involved in binding of synthetic hexa- and octapeptide analogs of somatostatin. A phenylalanine within this region is esp. crit. for binding octapeptide analogs such as Sandostatin. The third intracellular loop of this receptor may be particularly important in coupling the receptor to G proteins and appears to contain sites that may be involved in the desensitization of the receptor. In fact, this receptor becomes phosphorylated during desensitization. Phosphorylation of sites within the third intracellular loop of the receptor may be responsible for uncoupling the receptor from G proteins and cellular effector systems. Biochem. studies have revealed which G proteins assoc. with this receptor and have indicated that different G proteins link the receptor to distinct cellular effector systems. Because of the important physiol. roles of this receptor and its involvement in mediating therapeutic actions of somatostatin analogs, non-**peptide** SSTR2 drugs may have a no. of clin. uses. Structure-function anal. of this receptor may facilitate the development of these drugs.

L6 ANSWER 23 OF 27 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1996:482077 HCAPLUS
DOCUMENT NUMBER: 125:185921
TITLE: Molecular control of **peptide** hormone and receptor expression
AUTHOR(S): Dimaline, Rod
CORPORATE SOURCE: Physiological Laboratory, University Liverpool, Liverpool, L69 3BX, UK
SOURCE: Proceedings of the Nutrition Society (1996), 55(1B), 265-277
CODEN: PNUSA4; ISSN: 0029-6651
PUBLISHER: Cambridge University Press
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review, with 77 refs., on the 2 aspects of gastric endocrine cell gene expression: first, the rapid changes in gene expression that occur within a few min to a few h of ingestion of food or in response to changes in gastric lumen pH; and second, more slowly developing (days to weeks) adaptive changes that occur in response to chronic changes in the innervation of the stomach. The rapid changes were discussed in the context of the physiol. control of gastric acid secretion and the long-term changes were related to gastric mucosal protection. In addn., the expression and **regulation** of hormone receptors were discussed with ref. to somatostatin.

L6 ANSWER 24 OF 27 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1996:267409 HCAPLUS
DOCUMENT NUMBER: 124:312943
TITLE: Gastric secretion
AUTHOR(S): Schubert, Mitchell L.
CORPORATE SOURCE: Medical College of Virginia, Richmond, VA, USA
SOURCE: Current Opinion in Gastroenterology (1995), 11(6),

469-78
CODEN: COGAEK; ISSN: 0267-1379
PUBLISHER: Rapid Science Publishers
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English
AB A review, with 106 refs. This review of the past year's literature focuses on progress in the elucidation of the pathways and mechanisms controlling gastric exocrine (ie, acid and pepsin) and endocrine (ie, gastrin, histamine, and somatostatin) secretion at central, peripheral, and intracellular levels by neural, hormonal, and paracrine agents. Mol. biol. and immunocytochem. techniques coupled with physiol. studies have furthered the authors' understanding of the pathways and mechanisms **regulating** gastric secretions. At least three subtypes of muscarinic receptors, five subtypes of **somatostatin receptors**, and three subtypes of gastrin receptors have been identified, several of which participate in the **regulation** of acid secretion. γ-Aminobutyric acid has been identified convincingly in antral gastrin cells and tentatively in somatostatin-contg. D and serotonin-contg. enterochromaffin cells. Strong evidence supports the role of cholecystokinin and secretin as physiol. enterogastrones. Traditionally considered hormones, these **peptides** may inhibit acid secretion predominantly via vagal afferent nerve fibers. Cytoskeletal and low mol. mass GTP-binding proteins may participate in the **regulation** of membrane trafficking in parietal and chief cells.

L6 ANSWER 25 OF 27 HCAPLUS COPYRIGHT 2004 ACS on STN
Full Text | Citing References
ACCESSION NUMBER: 1991:670714 HCAPLUS
DOCUMENT NUMBER: 115:270714
TITLE: Cellular receptors implicated in epithelial transport
AUTHOR(S): Ruszniewski, P.
CORPORATE SOURCE: Serv. Gastroenterol., Hop. Bichat, Paris, F-75877, Fr.
SOURCE: Gastroenterologie Clinique et Biologique (1990), 14(12 bis), 29D-31D
CODEN: GCBIDC; ISSN: 0399-8320
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: French
AB A review, with 9 refs., of the role of **peptide** hormone receptors in intestinal epithelium transport. Specific topics discussed were expression of receptors during differentiation, gastrin and cholecystokinin receptors in gastric mucous membrane, receptors for **peptides** of the enteroglucagon family, and **somatostatin receptors**.

L6 ANSWER 26 OF 27 HCAPLUS COPYRIGHT 2004 ACS on STN
Full Text | Citing References
ACCESSION NUMBER: 1986:491447 HCAPLUS
DOCUMENT NUMBER: 105:91447
TITLE: **Regulation** of pancreatic acinar receptors by **peptides**
AUTHOR(S): Moessner, Joachim; Fischbach, Wolfgang
CORPORATE SOURCE: Med. Poliklin., Julius-Maximilians-Univ., Wuerzburg, D-8700, Fed. Rep. Ger.
SOURCE: Klinische Wochenschrift (1986), 64(11), 489-98
CODEN: KLWOAZ; ISSN: 0023-2173
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: German
AB A review, with 63 refs., on the **regulation** of pancreatic acinar receptors by **peptides**. The **peptides** may act on the same receptor they **regulate** or on other receptors causing **regulation** via receptor interactions. E.g., cholecystokinin causes desensitization of its own

receptor but also affects the **somatostatin receptor** capacity and affinity, the internalization of insulin-like growth factor and EGF receptors, and insulin receptor/cholecytokinin receptor interactions.

L6 ANSWER 27 OF 27 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1981:96391 HCAPLUS
DOCUMENT NUMBER: 94:96391
TITLE: **Regulation** of **peptide** receptors by homologous and heterologous ligands in cultured pituitary cells
AUTHOR(S): Schonbrunn, Agnes; Tashjian, Armen H., Jr.
CORPORATE SOURCE: Lab. Toxicol., Harvard Sch. Public Health, Boston, MA, 02115, USA
SOURCE: Endocrinol. Proc. Int. Congr. Endocrinol., 6th (1980), 579-82. Editor(s): Cumming, Ian A.; Funder, John W.; Mendelsohn, Frederick A. O. Elsevier/N. Holland Biomed. Press: Amsterdam, Neth.
CODEN: 44YLAV
DOCUMENT TYPE: Conference; **General Review**
LANGUAGE: English
AB A review with 12 refs. on the **regulation** of TRH [24305-27-9], somatostatin [51110-01-1], and epidermal growth factor [62229-50-9] receptors by homologous ligand of heterologous **peptides** in cultured somatotrophs.

=> **d his**

(FILE 'HOME' ENTERED AT 17:27:34 ON 07 MAY 2004)

FILE 'HCAPLUS' ENTERED AT 17:27:42 ON 07 MAY 2004
L1 2507 S SOMATOSTATIN () RECEPTOR?
L2 614 S L1 AND REGULAT?
L3 1 S L2 AND PEPTI? () COMPOUND?
L4 224 S L2 AND PEPTI?
L5 219 S L2 AND PEPTIDE?
L6 27 S L5 AND REVIEW/DT
L7 0 S L6 AND DUPLICATE REMOVE

=> **s l2 and diabete?**
88595 DIABETE?
L8 13 L2 AND DIABETE?

=> **s l8 and review/dt**
1723637 REVIEW/DT
L9 2 L8 AND REVIEW/DT

=> **d l9, ibib abs fhitstr, 1-2**

L9 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2002:415139 HCAPLUS
DOCUMENT NUMBER: 137:211012
TITLE: New somatostatin analogs: Will they fulfil old promises?
AUTHOR(S): Lamberts, S. W. J.; van der Lely, A. J.; Hofland, L. J.
CORPORATE SOURCE: Department of Medicine, Erasmus Medical Centre,

Rotterdam, 3015 GD, Neth.
SOURCE: European Journal of Endocrinology (2002), 146(5), 701-705
CODEN: EJOEEP; ISSN: 0804-4643
PUBLISHER: BioScientifica Ltd.
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English
AB A review discusses the development of somatostatin analogs, which play an inhibitory role in the **regulation** of several organ systems in man and other species, such as the central nervous system, the hypothalamus, and the pituitary gland, the gastrointestinal tract, the endocrine and exocrine pancreas, several components of the immune system, the retina, and vessel walls. The new developments in **somatostatin receptor** physiol. and the potential role of somatostatin analogs in the glycemic and metabolic control of **diabetes** mellitus and in the treatment of cancer are tackled. The use and characteristics of universal ligand, SOM-230, is also described.
REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1992:509059 HCAPLUS
DOCUMENT NUMBER: 117:109059
TITLE: Molecular biology of pancreatic β cells. Recent topics
AUTHOR(S): Seino, Susumu
CORPORATE SOURCE: Sch. Med., Chiba Univ., Chiba, 280, Japan
SOURCE: Saishin Igaku (1992), 47(6), 1053-7
CODEN: SAIGAK; ISSN: 0370-8241
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: Japanese
AB A review with 19 refs. on **regulation** of insulin secretion by pancreatic β cells focusing on glucose sensors (GLUT2 protein and glucokinase) and their abnormalities at the genetic level in **diabetes**, and Ca2+ signaling mediated by voltage-dependent Ca2+ channels, inositol trisphosphate receptors, and **somatostatin receptors**.

=> **d his**

(FILE 'HOME' ENTERED AT 17:27:34 ON 07 MAY 2004)

FILE 'HCAPLUS' ENTERED AT 17:27:42 ON 07 MAY 2004
L1 2507 S SOMATOSTATIN () RECEPTOR?
L2 614 S L1 AND REGULAT?
L3 1 S L2 AND PEPTI? () COMPOUND?
L4 224 S L2 AND PEPTI?
L5 219 S L2 AND PEPTIDE?
L6 27 S L5 AND REVIEW/DT
L7 0 S L6 AND DUPLICATE REMOVE
L8 13 S L2 AND DIABETE?
L9 2 S L8 AND REVIEW/DT

=> **s l2 and obes?**
30855 OBES?
L10 8 L2 AND OBES?

=> **s l10 and review/dt**

```
       1723637 REVIEW/DT
L11          0 L10 AND REVIEW/DT

=> d l10, ibib abs fhitstr, 1-8
```

L10 ANSWER 1 OF 8 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2003:532691 HCAPLUS
DOCUMENT NUMBER: 139:95435
TITLE: Modified receptors on cell membranes for the discovery of therapeutic ligands
INVENTOR(S): Schwartz, Thue W.; Martini, Lene; Heydorn, Arne; Jorgensen, Rasmus
PATENT ASSIGNEE(S): 7TM Pharma A/S, Den.
SOURCE: PCT Int. Appl., 122 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003055914	A2	20030710	WO 2002-DK900	20021220
WO 2003055914	A3	20031023		

W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:

DK 2001-1944	A	20011221
DK 2002-113	A	20020122
DK 2002-1043	A	20020703
US 2002-394122P	P	20020703

AB A drug discovery method is provided for selecting a compd. selected from the group consisting of a small org. substance, a biopharmaceutical, or an antibody or part thereof. The method comprises the steps of (i) expressing one or more receptors on a cell membrane, such as, e.g., an exterior cell surface of a cell, (ii) contacting one or more expressed receptors with a test compd. or a selection of test compds. (libraries), and (iii) selecting one or more compds. based on its ability to bind one or more receptors. The step of expressing the one or more receptors comprises capturing one or more receptors on the exterior cell surface in a conformation that predominantly enables binding or interaction with a ligand, and the conformation that predominantly enables binding or interaction with a ligand is provided by modification of one or more receptors by a method comprising at least one of the following: (a) fusion with any protein which keeps the receptor in the desired conformation such as, e.g. an arrestin, a modified arrestin, a G-protein or a modified G-protein, (b) site-directed mutagenesis, and (c) deletion. The receptors may be captured on the exterior cell surface by at least one of the following: (d) interaction of the receptor with a scaffolding protein, optionally, with a scaffolding protein network and (e) means for blocking

receptor internalization, e.g. by co-expression of a mutated dynamin or a modified arrestin or by use of chems. such as, e.g., sucrose and/or Tris. Thus, by coexpressing of either the wild-type receptor or by modifying the receptor by engineering for example a recognition motif for a strong binder into its structure (for example, a PDZ recognition motif at its C-terminal end), and coexpression of this with a scaffolding protein such as PSD-95 or a modified scaffolding protein which interacts with the cytoskeleton at the cell surface or is made to be closely assocd. with the membrane through a lipid anchor, a high level of surface expression can be ensured, which will benefit its use in the drug discovery process. As a result of the strong tendency of the scaffolding proteins to interact with each other, just the cotransfection with one or more appropriate scaffolding proteins or modified scaffolding protein may also lead to the formation of patches with high local concns of the receptor or modified receptor, which will be highly beneficial in the drug discovery process where they are used initially to select binding mols. The method is exemplified by expression of the NK1 receptor in an agonist high-affinity binding form at the surface of transfected cells through fusion with arrestin or the N-terminal fragment of arrestin.

L10 ANSWER 2 OF 8 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2003:61729 HCAPLUS
DOCUMENT NUMBER: 138:297943
TITLE: **Somatostatin receptor** subtype 5 **regulates** insulin secretion and glucose homeostasis
AUTHOR(S): Strowski, Mathias Z.; Kohler, Martin; Chen, Howard Y.; Trumbauer, Myrna E.; Li, Zhihua; Szalkowski, Deborah; Gopal-Truter, Shobhna; Fisher, Jill K.; Schaeffer, James M.; Blake, Allan D.; Zhang, Bei B.; Wilkinson, Hilary A.
CORPORATE SOURCE: Department of Molecular Endocrinology, Merck Research Laboratories, Rahway, NJ, 07065, USA
SOURCE: Molecular Endocrinology (2003), 17(1), 93-106
CODEN: MOENEN; ISSN: 0888-8809
PUBLISHER: Endocrine Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Somatostatin (SRIF) **regulates** pancreatic insulin and glucagon secretion. In the present study the authors describe the generation of SRIF receptor subtype 5 knockout (sst5 KO) mice to examine the role of SRIF receptor subtypes (sst) in **regulating** insulin secretion and glucose homeostasis. Mice deficient in sst5 were viable, fertile, appeared healthy, and displayed no obvious phenotypic abnormalities. Pancreatic islets isolated from sst5 KO mice displayed increased total insulin content as compared with islets obtained from wild-type (WT) mice. Somatostatin-28 (SRIF-28) and the sst5/sst1-selective agonist compd. 5/1 potently inhibited glucose-stimulated insulin secretion from WT islets. SRIF-28 inhibited insulin secretion from sst5 KO islets with 16-fold less potency while the maximal effect of compd. 5/1 was markedly diminished when compared with its effects in WT islets. Sst5 KO mice exhibited decreased blood glucose and plasma insulin levels and increased leptin and glucagon concns. compared with WT mice. Furthermore, sst5 KO mice displayed decreased susceptibility to high fat diet-induced insulin resistance. The results of these studies suggest sst5 mediates SRIF inhibition of pancreatic insulin secretion and contributes to the **regulation** of glucose homeostasis and insulin sensitivity. The authors' findings suggest a potential beneficial role of sst5 antagonists for alleviating metabolic abnormalities assocd. with **obesity** and insulin resistance.

REFERENCE COUNT: 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 3 OF 8 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2003:42303 HCAPLUS
DOCUMENT NUMBER: 138:102018
TITLE: Sequences of novel human **somatostatin receptor**-like proteins and uses in diagnosis, therapy and drug screening
INVENTOR(S): Ramakrishnan, Shyam
PATENT ASSIGNEE(S): Bayer Aktiengesellschaft, Germany
SOURCE: PCT Int. Appl., 155 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003004530	A1	20030116	WO 2001-EP7737	20010706
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
WO 2003004531	A2	20030116	WO 2002-EP7564	20020708
WO 2003004531	A3	20031204		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.: WO 2001-EP7737 W 20010706

AB The invention provides protein and cDNA sequences of novel human **somatostatin receptor**-like proteins. Reagents which **regulate** human **somatostatin receptor**-like protein and reagents which bind to human **somatostatin receptor**-like gene products can be used to **regulate** the effect of somatostatin. Human tumors which possess **somatostatin receptors**, such as pituitary tumors, endocrine pancreatic tumors, carcinoids, APUDomas such as paragangliomas, pheochromocytomas, medullary thyroid carcinomas, and small cell lung cancer, neuroblastomas, brain tumors such as meningiomas and glial-derived brain tumors, Merkel cell tumors, breast cancer, adenocarcinomas, and lymphomas, can be treated.

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 4 OF 8 HCAPLUS COPYRIGHT 2004 ACS on STN

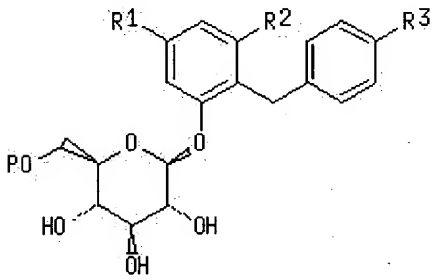
Full Text | Citing References

ACCESSION NUMBER: 2002:637688 HCAPLUS
DOCUMENT NUMBER: 137:185757
TITLE: Preparation of glucopyranosyloxybenzylbenzene derivatives as inhibitors of human SGLT2 (sodium-dependent glucose-transporter 2) activity and medicinal use thereof
INVENTOR(S): Fushimi, Nobuhiko; Tatani, Kazuya; Fujikura, Hideki; Nishimura, Toshihiro; Fujioka, Minoru; Nakabayashi, Takeshi; Isaji, Masayuki
PATENT ASSIGNEE(S): Kissei Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 145 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002064606	A1	20020822	WO 2002-JP1178	20020213
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1367060	A1	20031203	EP 2002-701540	20020213
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

PRIORITY APPLN. INFO.: JP 2001-37729 A 20010214
WO 2002-JP1178 W 20020213

OTHER SOURCE(S): MARPAT 137:185757
GI



I

AB 2-Benzylphenyl β-D-glucopyranoside derivs. represented by the following general formula (I) and pharmacol. acceptable salts thereof [wherein P = H, a group constituting a prodrug; R1 = H, NH2, mono- or di(lower alkyl)amino, carbamoyl, lower alkyl, lower alkoxy, lower alkoxy-lower alkyl, lower alkoxy-lower alkoxy, carbamoyl-lower alkyl, carboxy-lower alkoxy, P1-O-A1- (wherein P1 = H, a group constituting a prodrug; A1 = a single bond, lower alkylene or alkyleneoxy); R2 = H, lower

alkyl; R3 = lower alkyl, lower alkoxy, lower alkylthio, lower alkenyloxy, aralkyloxy, lower alkoxy-lower alkyl, lower alkoxy-lower alkoxy, lower alkoxy-lower alkylthio, CO2H, lower alkoxycarbonyl, cyano, aralkyloxy-lower alkyl, cyano-lower alkyl, CONH2, carbamoyl-lower alkyl, NH2, mono- or di(lower alkyl)amino, lower alkoxycarbonyl-lower alkyl, carboxy-lower alkoxy, P2-O-A2- (wherein P2 = H, a group constituting a prodrug; A2 - lower alkylene, lower alkyleneoxy, lower alkylenethio, lower alkenylene); some provisos are given] are prepd. These compds. are useful as preventives or remedies for diseases caused by hyperglycemia such as diabetes, diabetes complications, **obesity**, hyperinsulinism, glucose metab., hyperlipidemia, hypercholesteremia, hypertriglycemia, abnormal lipid metab., atherosclerosis, hypertension, ischemic heart failure, edema, hyperuricemia, and gout because of having an improved oral absorbability and exerting an excellent human SGLT2 activity inhibitory effect (in vivo). Thus, 0.037 mL Et chloroformate was added to a soln. of 0.075 g 2-(4-ethylbenzyl)-5-hydroxymethylphenyl β-D-glucopyranoside in 2 mL 2,4,6-trimethylpyridine and stirred at room temp. for 17 h to give 0.020 g 2-(4-ethylbenzyl)-5-hydroxymethylphenyl 6-O-ethoxycarbonyl-β-D-glucopyranoside (II). Oral bioavailability (serum concn.) of II was 43% of that of i.v. administration in SD rats. II increased the excretion of glucose in urine from 7.0 mg/24 h/200 g body wt. at 1 mg/kg body wt. to 195 mg/24 h/200 g body wt. at 10 mg/kg body wt. when fed p.o. to SD rats.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 5 OF 8 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2002:10426 HCAPLUS
DOCUMENT NUMBER: 136:85822
TITLE: Preparation of biphenylcarboxamide compounds as GPR14 antagonists or **somatostatin receptor regulators**
INVENTOR(S): Tarui, Naoki; Santo, Takashi; Watanabe, Hiroyuki; Aso, Kazuyoshi; Miwa, Tetsuo; Takekawa, Shiro
PATENT ASSIGNEE(S): Takeda Chemical Industries, Ltd., Japan
SOURCE: PCT Int. Appl., 274 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

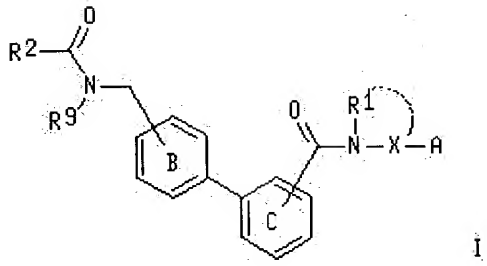
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002000606	A1	20020103	WO 2001-JP5541	20010628
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 2001066346	A5	20020108	AU 2001-66346	20010628
JP 2002080439	A2	20020319	JP 2001-196645	20010628
EP 1295867	A1	20030326	EP 2001-943851	20010628
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

PRIORITY APPLN. INFO.: JP 2000-200118 A 20000628

WO 2001-JP5541 W 20010628

OTHER SOURCE(S): MARPAT 136:85822

GI



I

AB The title compds. (I) or salts thereof [wherein R1 represents hydrogen or (un)substituted hydrocarbyl; X represents a spacer having a 1 to 12 atom linear chain moiety; A represents (un)substituted amino or N-heterocyclyl; R2 represents (un)substituted hydrocarbyl or amino; and R3 represents (un)substituted hydrocarbyl; ring B and C represent an optionally further substituted benzene ring], which have an antagonism against urotensin II receptor GPR14 (orphan receptor), are prepd. These compds. are also somatostatin, in particular somatostatin 5 receptor-function **regulators** such as **somatostatin receptor** agonists and antagonists and are useful for the prevention and treatment of hypertension, arteriosclerosis, cardiac hypertrophy, myocardial infarction, diabetes, **obesity**, diabetes complications, central diseases, digestive tract diseases, glaucoma, acromegaly, or tumor. Thus, 3'-[[2-[4-(aminosulfonyl)phenyl]ethyl]aminomethyl]-N-[2-(1-pyrrolidinyl)ethyl]-1,1'-biphenyl-3-carboxamide was condensed with trans-cinnamic acid using 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride and 1-hydroxybenzoriazole in CH2Cl2 and DMF at room temp. for 18 h to give 3'-[[N-[2-[4-(aminosulfonyl)phenyl]ethyl]-N-[(E)-3-phenyl-2-propenoyl]amino]methyl]-N-[2-(1-pyrrolidinyl)ethyl]-1,1'-biphenyl-3-carboxamide (II). N-(2-aminoethyl)-3'-[[N-[4-(aminosulfonyl)benzoyl]-N-(1-naphthylmethyl)amino]methyl]-1,1'-biphenyl-2-carboxamide trifluoroacetate and N-(2-aminoethyl)-3'-[[N-[4-[[[amino(imino)methyl]amino]methyl]benzoyl]-N-(1-naphthylmethyl)amino]methyl]-1,1'-biphenyl-2-carboxamide trifluoroacetate showed IC50 of 3 and 6 nM for inhibiting the binding of [125I]-somatostatin to CHO cell line expressing human somatostatin 5 receptor. A capsule and a tablet formulation contg. II were prepd.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 6 OF 8 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

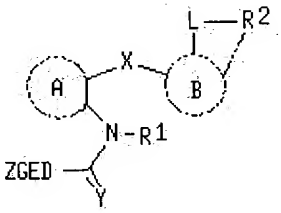
ACCESSION NUMBER: 2000:277959 HCAPLUS
DOCUMENT NUMBER: 132:321662
TITLE: Preparation of aromatic amine derivatives and agents containing the same
INVENTOR(S): Oi, Satoru; Suzuki, Nobuhiro; Aso, Kazuyoshi; Banno, Yoshihiro
PATENT ASSIGNEE(S): Takeda Chemical Industries, Ltd., Japan
SOURCE: PCT Int. Appl., 309 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000023420	A1	20000427	WO 1999-JP5755	19991019
W: AE, AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CR, CU, CZ, DM, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MA, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9961246	A1	20000508	AU 1999-61246	19991019
JP 2000191615	A2	20000711	JP 1999-297129	19991019
EP 1123918	A1	20010816	EP 1999-947962	19991019
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

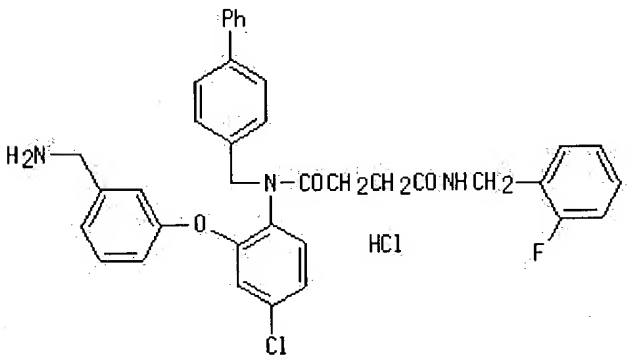
PRIORITY APPLN. INFO.: JP 1998-298940 A 19981020
WO 1999-JP5755 W 19991019

OTHER SOURCE(S): MARPAT 132:321662

GI



I



II

AB Title compds. [I; wherein A is an optionally substituted arom. ring; B is an optionally substituted cyclic hydrocarbon oxy group; Z is an optionally substituted cyclic hydrocarbon group; R1 is hydrogen, optionally substituted hydrocarbyl, an optionally substituted heterocyclic group, or acyl; R2 is optionally substituted amino; D is a free valency or a divalent group; E is CO, CON(Ra), COO, N(Ra)CON(Rb), N(Ra)SO2, N(Ra), O, S, SO, SO2; G is a free valency or a divalent group; L is a free valency, an optionally substituted divalent hydrocarbon group which may be interrupted by O or S, or the like; X is oxygen, optionally oxidized sulfur, optionally substituted nitrogen, or an optionally substituted divalent hydrocarbon group; Y is two hydrogen atoms, oxygen, or sulfur; and the dotted line indicates that R2 and an atom on ring B may together form a ring] and salts are prepd. and tested as **somatostatin receptor**

regulators. Thus, the title compd. II was prepd. in treatment or prevention of diabetes and **obesity**.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 7 OF 8 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1999:114431 HCAPLUS
DOCUMENT NUMBER: 130:148923
TITLE: Role of growth hormone (GH)-releasing hormone and somatostatin on leptin-induced GH secretion
AUTHOR(S): Carro, E.; Senaris, R. M.; Seoane, L. M.; Frohmann, L. A.; Arimura, A.; Casanueva, F. F.; Dieguez, C.
CORPORATE SOURCE: Dep. Physiology, Fac. Medicine, Univ. Santiago de Compostela, Santiago de Compostela, E-15700, Spain
SOURCE: Neuroendocrinology (1999), 69(1), 3-10
CODEN: NUNDAJ; ISSN: 0028-3835
PUBLISHER: S. Karger AG
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Leptin is a hormone secreted by the adipocytes that **regulates** food intake and energy expenditure. It is known that growth hormone (GH) secretion is markedly influenced by body wt., being suppressed in **obesity** and cachexia, and recent data have demonstrated that GH release is **regulated** by leptin levels. Although 1 of the sites of action of leptin is likely to be the hypothalamus, since leptin receptor mRNA is particularly abundant in several hypothalamic nuclei, the mechanisms by which leptin **regulates** GH secretion are not yet known. The aim of the present study was to investigate whether leptin could act at the hypothalamic level modulating somatostatin and GH-releasing hormone (GHRH) expression. The administration of anti-GHRH serum (500 μL, i.v.) completely blocked leptin-induced GH release in fasting rats. In contrast, the treatment with anti-somatostatin serum (500 μL, i.v.) increased GH release in this condition. Furthermore, leptin administration (10 μg, i.c.v.) to intact fasting animals reversed the inhibitory effect produced by fasting on GHRH mRNA levels in the arcuate nucleus of the hypothalamus, and increased somatostatin mRNA content in the periventricular nucleus. Finally, leptin administration (10 μg, i.c.v.) to hypophysectomized fasting rats increased GHRH mRNA levels, and decreased somatostatin mRNA content, indicating an effect of leptin on hypothalamic GHRH- and somatostatin-producing neurons. These findings suggest a role for GHRH and somatostatin as mediators of leptin-induced GH secretion.

REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 8 OF 8 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1992:4675 HCAPLUS
DOCUMENT NUMBER: 116:4675
TITLE: Alteration of somatostatin but not growth hormone-releasing factor pituitary binding sites in **obese** Zucker rats
AUTHOR(S): Abribat, Thierry; Finkelstein, Judith A.; Gaudreau, Pierrette
CORPORATE SOURCE: Neuroendocrinol. Lab., Notre-Dame Hosp. Res. Cent., Montreal, QC, H2L 4K8, Can.

SOURCE: Regulatory Peptides (1991), 36(2), 263-70
CODEN: REPPDY; ISSN: 0167-0115
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The present study was designed to det. whether the diminution of growth hormone (GH) secretion that occurs in **obese** Zucker rats is related to alterations of GH-releasing factor (GRF) or somatostatin (SRIF) pituitary binding sites. Cold satn. studies were performed in pituitary homogenates of 4-mo-old lean and **obese** rats, using [125I-Tyr10]hGRF(1-44)NH2 as radioligand and [127I-Tyr10]hGRF(1-44)NH2 as competitor, and in pituitary membrane prepns., using [125I-Tyr0,D-Trp8]SRIF14 as radioligand and [127I-Tyr0,D-Trp8]SRIF14 as competitor. In lean rats, anal. of the curves by the Ligand program revealed the presence of two distinct classes of GRF binding sites, the first being of high affinity (0.74 nM) and low capacity (118 fmol/mg protein), the second being of lower affinity (880 nM) and higher capacity (140 pmol/mg protein), and of a single class of SRIF binding sites (affinity: 0.40 nM; capacity: 24 fmol/mg protein). In **obese** rats, no difference was obsd. in GRF binding parameters for both classes of sites, but the concn. of somatostatin binding sites was reduced by 67% when compared to their lean littermates. These findings suggest that the SRIF pituitary receptors are down-**regulated** in **obese** Zucker rats and indicate that no alteration of GRF pituitary binding sites contribute to the blunted GH secretion obsd. in this model of **obesity**.

```
=> d his

     (FILE 'HOME' ENTERED AT 17:27:34 ON 07 MAY 2004)

     FILE 'HCAPLUS' ENTERED AT 17:27:42 ON 07 MAY 2004
L1          2507 S SOMATOSTATIN () RECEPTOR?
L2           614 S L1 AND REGULAT?
L3             1 S L2 AND PEPTI? () COMPOUND?
L4           224 S L2 AND PEPTI?
L5           219 S L2 AND PEPTIDE?
L6            27 S L5 AND REVIEW/DT
L7             0 S L6 AND DUPLICATE REMOVE
L8            13 S L2 AND DIABETE?
L9             2 S L8 AND REVIEW/DT
L10            8 S L2 AND OBES?
L11            0 S L10 AND REVIEW/DT

=> s l8 and complic?
         90801 COMPLIC?
L12          2 L8 AND COMPLIC?

=> s l12 and review/dt
       1723637 REVIEW/DT
L13          0 L12 AND REVIEW/DT

=> d his

     (FILE 'HOME' ENTERED AT 17:27:34 ON 07 MAY 2004)

     FILE 'HCAPLUS' ENTERED AT 17:27:42 ON 07 MAY 2004
L1          2507 S SOMATOSTATIN () RECEPTOR?
L2           614 S L1 AND REGULAT?
L3             1 S L2 AND PEPTI? () COMPOUND?
L4           224 S L2 AND PEPTI?
L5           219 S L2 AND PEPTIDE?
```

```
L6            27 S L5 AND REVIEW/DT
L7             0 S L6 AND DUPLICATE REMOVE
L8            13 S L2 AND DIABETE?
L9             2 S L8 AND REVIEW/DT
L10            8 S L2 AND OBES?
L11            0 S L10 AND REVIEW/DT
L12            2 S L8 AND COMPLIC?
L13            0 S L12 AND REVIEW/DT

=> s l2 and intract? () diarrhe?
          2611 INTRACT?
         15577 DIARRHE?
            30 INTRACT? (W) DIARRHE?
L14          0 L2 AND INTRACT? (W) DIARRHE?

=> s l2 and diarrhe?
         15577 DIARRHE?
L15          1 L2 AND DIARRHE?

=> s l15 and review/dt
       1723637 REVIEW/DT
L16          1 L15 AND REVIEW/DT

=> d l16, ibib abs fhitstr, 1

L16  ANSWER 1 OF 1  HCAPLUS  COPYRIGHT 2004 ACS on STN
```

Full Text | Citing References

ACCESSION NUMBER: 2002:74204 HCAPLUS
DOCUMENT NUMBER: 136:350603
TITLE: Review: Somatostatin and intestinal schistosomiasis: Therapeutic and neuropathological implications in host-parasite interactions
AUTHOR(S): Chatterjee, Shyama; De Man, Joris; Van Marck, Eric
CORPORATE SOURCE: Pathology Unit, Department of Medicine, University of Antwerp, Wilrijk, 2610, Belg.
SOURCE: Tropical Medicine & International Health (2001), 6(12), 1008-1015
CODEN: TMIHFL; ISSN: 1360-2276
PUBLISHER: Blackwell Science Ltd.
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review. A better insight into the mechanisms **regulating** the human body can lead to improved knowledge of the patho-physiol. processes of many diseases. New therapeutic possibilities can be devised at the level of these **regulatory** mechanisms. Somatostatin is one of the major **regulatory** hormones in the central nervous system (CNS) and digestive system. Its wide variety of activities means it is implicated in a broad range of conditions. One symptom common to both the acute and chronic stages of schistosomiasis is intestinal pathol. characterized by abdominal pain, **diarrhea** that is bloody in more chronic stages, nausea and fever. Some chronic patients develop severe hepatosplenic fibrosis, leading to fatal esophageal variceal bleeding. In this review we assess the therapeutic potential of somatostatin in the treatment of intestinal pathol. assocd. with schistosomiasis. The activity of somatostatin is mediated via binding to specific cell surface receptors. While we are making progress in studies of the expression and **regulation** of the different **somatostatin receptors**, the true role and distribution of each receptor subtype is far from fully understood. Animal models will help to define the specific role of individual receptors in physiol. and

pathol. conditions. The **regulation** of receptor expression as well as receptor internalization can give us insight into the effect of exogenous somatostatin on schistosomiasis-mediated intestinal pathol., as well as its modulation by intrinsically produced somatostatin levels.

REFERENCE COUNT: 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=>

```
* * * * * * * * * *   Welcome to STN International   * * * * * * * * * *

 NEWS  1           Web Page URLs for STN Seminar Schedule - N. America
 NEWS  2           "Ask CAS" for self-help around the clock
 NEWS  3  JAN 27   Source of Registration (SR) information in REGISTRY updated
                   and searchable
 NEWS  4  JAN 27   A new search aid, the Company Name Thesaurus, available in
                   CA/CAplus
 NEWS  5  FEB 05   German (DE) application and patent publication number format
                   changes
 NEWS  6  MAR 03   MEDLINE and LMEDLINE reloaded
 NEWS  7  MAR 03   MEDLINE file segment of TOXCENTER reloaded
 NEWS  8  MAR 03   FRANCEPAT now available on STN
 NEWS  9  MAR 29   Pharmaceutical Substances (PS) now available on STN
 NEWS 10  MAR 29   WPIFV now available on STN
 NEWS 11  MAR 29   No connect hour charges in WPIFV until May 1, 2004
 NEWS 12  MAR 29   New monthly current-awareness alert (SDI) frequency in RAPRA
 NEWS 13  APR 26   PROMT: New display field available
 NEWS 14  APR 26   IFIPAT/IFIUDB/IFICDB: New super search and display field
                   available
 NEWS 15  APR 26   LITALERT now available on STN
 NEWS 16  APR 27   NLDB: New search and display fields available

 NEWS EXPRESS  MARCH 31 CURRENT WINDOWS VERSION IS V7.00A, CURRENT
               MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
               AND CURRENT DISCOVER FILE IS DATED 26 APRIL 2004
 NEWS HOURS    STN Operating Hours Plus Help Desk Availability
 NEWS INTER    General Internet Information
 NEWS LOGIN    Welcome Banner and News Items
 NEWS PHONE    Direct Dial and Telecommunication Network Access to STN
 NEWS WWW      CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that
specific topic.

  All use of STN is subject to the provisions of the STN Customer
  agreement.  Please note that this agreement limits use to scientific
  research.  Use for software development or design or implementation
  of commercial gateways or other similar uses is prohibited and may
  result in loss of user privileges and other penalties.

  * * * * * * * * * * * * * STN  Columbus  * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 16:33:18 ON 07 MAY 2004

=> file reg
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     0.21       0.21

FILE 'REGISTRY' ENTERED AT 16:33:55 ON 07 MAY 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2004 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:    5 MAY 2004  HIGHEST RN 680179-46-8
DICTIONARY FILE UPDATES:   5 MAY 2004  HIGHEST RN 680179-46-8
```

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2004

Please note that search-term pricing does apply when
conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=> **file uspatfull**

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.42	0.63

FILE 'USPATFULL' ENTERED AT 16:34:01 ON 07 MAY 2004
CA INDEXING COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)

FILE COVERS 1971 TO PATENT PUBLICATION DATE: 6 May 2004 (20040506/PD)
FILE LAST UPDATED: 6 May 2004 (20040506/ED)
HIGHEST GRANTED PATENT NUMBER: US6732373
HIGHEST APPLICATION PUBLICATION NUMBER: US2004088770
CA INDEXING IS CURRENT THROUGH 6 May 2004 (20040506/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 6 May 2004 (20040506/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Feb 2004
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Feb 2004

>>> USPAT2 is now available. USPATFULL contains full text of the <<<
>>> original, i.e., the earliest published granted patents or <<<
>>> applications. USPAT2 contains full text of the latest US <<<
>>> publications, starting in 2001, for the inventions covered in <<<
>>> USPATFULL. A USPATFULL record contains not only the original <<<
>>> published document but also a list of any subsequent <<<
>>> publications. The publication number, patent kind code, and <<<
>>> publication date for all the US publications for an invention <<<
>>> are displayed in the PI (Patent Information) field of USPATFULL <<<
>>> records and may be searched in standard search fields, e.g., /PN, <<<
>>> /PK, etc. <<<

>>> USPATFULL and USPAT2 can be accessed and searched together <<<
>>> through the new cluster USPATALL. Type FILE USPATALL to <<<
>>> enter this cluster. <<<
>>> <<<
>>> Use USPATALL when searching terms such as patent assignees, <<<
>>> classifications, or claims, that may potentially change from <<<
>>> the earliest to the latest publication. <<<

This file contains CAS Registry Numbers for easy and accurate
substance identification.

=> **s nichols, g?/au**
L1 94 NICHOLS, G?/AU

=> **s l1 and epoxide?**
40892 EPOXIDE?
L2 6 L1 AND EPOXIDE?

=> d l2, ibib abs fhitstr, 1-6

L2 ANSWER 1 OF 6 USPATFULL on STN

Full Text | Citing References

ACCESSION NUMBER: 2001:14546 USPATFULL
TITLE: Processes for preparing ink jet inks
INVENTOR(S): Cheng, Chieh-Min, Rochester, NY, United States
Nichols, Garland J., Ontario, NY, United States
Fu, Min-Hong, Webster, NY, United States
PATENT ASSIGNEE(S): Xerox Corporation, Stamford, CT, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6180691	B1	20010130
APPLICATION INFO.:	US 1999-365386		19990802 (9)

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Jagannathan, Vasu
ASSISTANT EXAMINER: Shosho, Callie E.
LEGAL REPRESENTATIVE: Palazzo, E. D.
NUMBER OF CLAIMS: 43
EXEMPLARY CLAIM: 1
LINE COUNT: 1543
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A process for the preparation of an ink which comprises mixing an ink vehicle, a colorant and a latex containing a polymer with epoxy groups, and wherein said latex is generated by the polymerization of a mixture of olefinic monomers, and wherein at least one of said olefinic monomers is an unsaturated **epoxide** monomer and which polymerization is accomplished in the presence of an anionic surfactant, and a nonionic surfactant.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L2 ANSWER 2 OF 6 USPATFULL on STN

Full Text | Citing References

ACCESSION NUMBER: 96:38948 USPATFULL
TITLE: Polymer foams with inherent nonflammability and thermal stability and methods of preparation thereof
INVENTOR(S): **Nichols, Gus**, 2501 Gulf-Freeway, #5, Dickinson, TX, United States 77539
Armeniades, C. D., 2127 Addison Rd., Houston, TX, United States 77030

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5514726		19960507
APPLICATION INFO.:	US 1992-945277		19920915 (7)

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Johnson, Rachel
LEGAL REPRESENTATIVE: Pravel, Hewitt, Kimball & Krieger
NUMBER OF CLAIMS: 8
EXEMPLARY CLAIM: 1
LINE COUNT: 1164
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Polymeric foams with novel chemical compositions are prepared by the

condensation of specially-synthesized precursors, which contain (in addition to carbon and hydrogen) one or more of the following elements: oxygen, fluorine, nitrogen (in structures with stable chemical bonds), silicon, boron, phosphorus (in high oxidation states), and certain metals (and/or their oxides and hydroxides). Upon mixing in the proper proportions and/or heating these precursors react rapidly to generate polymeric networks, consisting of heterocyclic crosslink centers, connected with heterochain segments; hydrogen is largely eliminated or replaced by fluorine. These structures possess inherent nonflammability and high thermoxidative stability. Foaming is effected by the gaseous by-products of the condensation reactions, as well as by the addition of foaming agents. The resulting foam products can be formulated to have a wide range of densities and flexibilities.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L2 ANSWER 3 OF 6 USPATFULL on STN

Full Text | Citing References

ACCESSION NUMBER: 88:27851 USPATFULL
TITLE: Liquid, solventless, complex polymeric compositions, thermosetting at ambient temperatures through addition polymerization mechanisms
INVENTOR(S): **Nichols, Gus**, 2501 Gulf Freeway, Unit 5, Dickinson, TX, United States 77539

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 4742147		19880503
APPLICATION INFO.:	US 1985-786738		19851011 (6)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1984-593591, filed on 26 Mar 1984, now patented, Pat. No. US 4547562
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Anderson, Harold D.
NUMBER OF CLAIMS: 6
EXEMPLARY CLAIM: 1
LINE COUNT: 1057
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Liquid, solventless, complex polymeric compositions are provided which thermoset at ambient temperatures through addition polymerization. In a preferred embodiment, a two component system includes a first component comprising amine or acrylate terminated polyurethanes, polyurethane-ureas or polyureas and a second component comprising di or polyacrylates. By adding an excess of acrylate, a one component system can be formed which thermosets when exposed to ultraviolet radiation.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L2 ANSWER 4 OF 6 USPATFULL on STN

Full Text | Citing References

ACCESSION NUMBER: 87:45176 USPATFULL
TITLE: Solventless polymeric composition reaction product of (1) adduct of amine and acrylate with (2) polyacrylate
INVENTOR(S): **Nichols, Gus**, 2501 Gulf Freeway, Building 18, Unit 5, Dickenson, TX, United States 77539

	NUMBER	KIND	DATE

PATENT INFORMATION: US 4675374 19870623
APPLICATION INFO.: US 1985-757511 19850718 (6)
RELATED APPLN. INFO.: Division of Ser. No. US 1984-593591, filed on 26 Mar 1984, now patented, Pat. No. US 4547562
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Anderson, Harold D.
LEGAL REPRESENTATIVE: Mosely, Neal J.
NUMBER OF CLAIMS: 13
EXEMPLARY CLAIM: 1
LINE COUNT: 1375
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Solventless polymeric compositions suitable for coatings and moldings are formed by the addition reaction product of a first component comprising mono, di or polyamines, or an adduct of mono, di or polyamines with mono, di or polyfunctional acrylates and/or **epoxides** and a second component comprising mono, di or polyacrylates or mixtures with mono, di or polyepoxides.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L2 ANSWER 5 OF 6 USPATFULL on STN

Full Text | Citing References

ACCESSION NUMBER: 87:38061 USPATFULL
TITLE: Use of aromatic amines for setting **epoxide** resins
INVENTOR(S): **Nichols, Gus**, 2501 Gulf Freeway, Bldg. 18, Unit 5, Dickinson, TX, United States 77539

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 4668757		19870526
APPLICATION INFO.:	US 1984-593592		19840326 (6)

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Nielsen, Earl
LEGAL REPRESENTATIVE: Mosely, Neal J.
NUMBER OF CLAIMS: 5
EXEMPLARY CLAIM: 1
LINE COUNT: 687
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Aromatic amines and their alkyl, amide, imide or amide-imide substituted derivatives in the presence of catalytic quantities of phenols, cresols, xylenols, bisphenols, and their like cause **epoxide** resins to thermoset at ambient temperatures. The resulting crosslinked polymers are useful for two component solution systems which provide corrosion and temperature resistant clear coatings or paints, and can also be used as solventless, liquid, two component systems for casting clear, pigmented or filled parts.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L2 ANSWER 6 OF 6 USPATFULL on STN

Full Text | Citing References

ACCESSION NUMBER: 85:61155 USPATFULL
TITLE: Solventless polymeric composition comprising non arylamine, polyacrylate and **epoxide**
INVENTOR(S): **Nichols, Gus**, 3500 Becker Dr. #8, Dickenson, TX, United States 77539

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 4547562		19851015	
APPLICATION INFO.:	US 1984-593591		19840326	(6)
DOCUMENT TYPE:	Utility			
FILE SEGMENT:	Granted			
PRIMARY EXAMINER:	Anderson, Harold D.			
LEGAL REPRESENTATIVE:	Arnold, White & Durkee			
NUMBER OF CLAIMS:	21			
EXEMPLARY CLAIM:	1			
LINE COUNT:	1413			

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Solventless polymeric compositions suitable for coatings and moldings are formed by the addition reaction product of a first component comprising mono, di or polyamines, or an adduct of mono, di or polyamines with mono, di or polyfunctional acrylates and/or **epoxides** and a second component comprising mono, di or polyacrylates or mixtures with mono, di or polyepoxides.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> **d his**

(FILE 'HOME' ENTERED AT 16:33:18 ON 07 MAY 2004)

FILE 'REGISTRY' ENTERED AT 16:33:55 ON 07 MAY 2004

FILE 'USPATFULL' ENTERED AT 16:34:01 ON 07 MAY 2004
L1 94 S NICHOLS, G?/AU
L2 6 S L1 AND EPOXIDE?

=> **file reg**

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	13.74	14.37

FILE 'REGISTRY' ENTERED AT 16:35:18 ON 07 MAY 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 5 MAY 2004 HIGHEST RN 680179-46-8
DICTIONARY FILE UPDATES: 5 MAY 2004 HIGHEST RN 680179-46-8

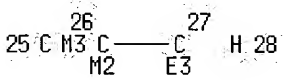
TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2004

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

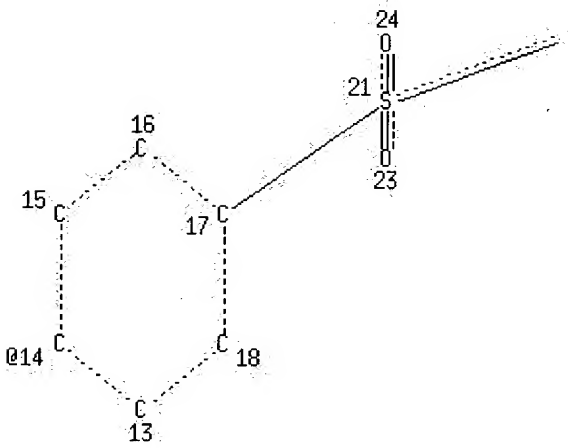
Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

```
=>
L3       STRUCTURE UPLOADED

=> d l3
L3 HAS NO ANSWERS
L3                  STR
```

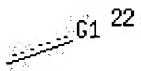


X @20

Page 1-A



Page 1-B

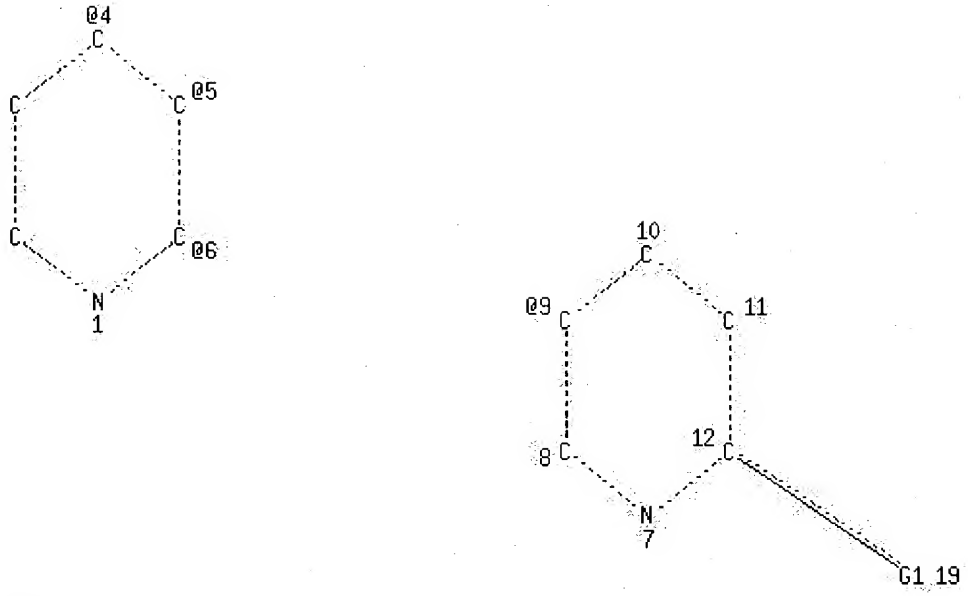


Page 1-C

@3

@2

Page 2-A



Page 2-B
VAR G1=25/26/28
VPA 20-2/3/4/5/6 S
VPA 14-4/5/6 S
VPA 9-2/5/6 S
NODE ATTRIBUTES:

HCOUNT	IS M3	AT	25
HCOUNT	IS M2	AT	26
HCOUNT	IS E3	AT	27
NSPEC	IS R	AT	1
NSPEC	IS R	AT	2
NSPEC	IS R	AT	3
NSPEC	IS R	AT	4
NSPEC	IS R	AT	5
NSPEC	IS R	AT	6
NSPEC	IS R	AT	7
NSPEC	IS R	AT	8
NSPEC	IS R	AT	9
NSPEC	IS R	AT	10
NSPEC	IS R	AT	11
NSPEC	IS R	AT	12
NSPEC	IS R	AT	13
NSPEC	IS R	AT	14
NSPEC	IS R	AT	15
NSPEC	IS R	AT	16
NSPEC	IS R	AT	17
NSPEC	IS R	AT	18
NSPEC	IS C	AT	19
NSPEC	IS C	AT	20
NSPEC	IS C	AT	21
NSPEC	IS C	AT	22
NSPEC	IS C	AT	23
NSPEC	IS C	AT	24

DEFAULT MLEVEL IS ATOM
MLEVEL IS CLASS AT 20 21 23 24 25 26 27 28
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC I
NUMBER OF NODES IS 28

```
STEREO ATTRIBUTES: NONE


=> s l3 and nichols, g?/au
COMBINATION OF STRUCTURE AND TEXT TERMS NOT VALID
The query entered contains both search terms created by
structure-building or screen commands and text search terms.  L#s
created via the STRUCTURE or SCREEN commands must be searched in the
structures files separately from text terms or profiles.  The L#
answer sets from structure searches can be used in crossover searches
and can be combined with text terms.

=> d his

     (FILE 'HOME' ENTERED AT 16:33:18 ON 07 MAY 2004)

     FILE 'REGISTRY' ENTERED AT 16:33:55 ON 07 MAY 2004

     FILE 'USPATFULL' ENTERED AT 16:34:01 ON 07 MAY 2004
L1            94 S NICHOLS, G?/AU
L2             6 S L1 AND EPOXIDE?

     FILE 'REGISTRY' ENTERED AT 16:35:18 ON 07 MAY 2004
L3               STRUCTURE UPLOADED

=> s l3 full
THE ESTIMATED SEARCH COST FOR FILE 'REGISTRY' IS 155.00 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N or END:y
FULL SEARCH INITIATED 16:35:57 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -  12108 TO ITERATE

100.0% PROCESSED   12108 ITERATIONS                              30 ANSWERS
SEARCH TIME: 00.00.01

L4            30 SEA SSS FUL L3

=> file hcaplus
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                   ENTRY    SESSION
FULL ESTIMATED COST                               155.42     169.79

FILE 'HCAPLUS' ENTERED AT 16:36:03 ON 07 MAY 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)


Copyright of the articles to which records in this database refer is
held by the publishers listed in the PUBLISHER (PB) field (available
for records published or updated in Chemical Abstracts after December
26, 1996), unless otherwise indicated in the original publications.
The CA Lexicon is the copyrighted intellectual property of the
the American Chemical Society and is provided to assist you in searching
databases on STN.  Any dissemination, distribution, copying, or storing
of this information, without the prior written consent of CAS, is
strictly prohibited.

FILE COVERS 1907 - 7 May 2004  VOL 140 ISS 20
FILE LAST UPDATED: 6 May 2004  (20040506/ED)
```

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> **s l4**
L5 176 L4

=> **s l4/prep**
176 L4
3144401 PREP/RL
L6 18 L4/PREP
(L4 (L) PREP/RL)

=> **s l6 and gus, n?/au**
0 GUS, N?/AU
L7 0 L6 AND GUS, N?/AU

=> **d l6, ibib abs fhitstr, 1-18**

L6 ANSWER 1 OF 18 HCAPLUS COPYRIGHT 2004 ACS on STN

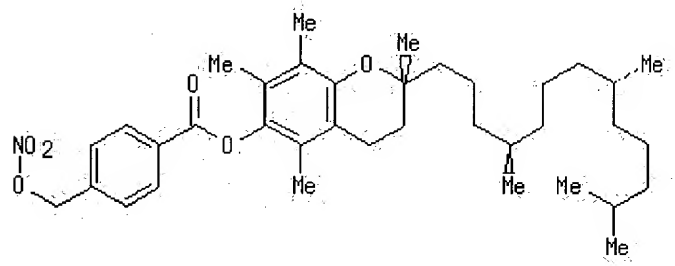
Full Text | Citing References

ACCESSION NUMBER: 2003:652131 HCAPLUS
DOCUMENT NUMBER: 139:214237
TITLE: Preparation of nitrate prodrugs able to release nitric oxide in a controlled and selective way and their use for prevention and treatment of inflammatory, ischemic and proliferative diseases
INVENTOR(S): Scaramuzzino, Giovanni
PATENT ASSIGNEE(S): Italy
SOURCE: Eur. Pat. Appl., 313 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1336602	A1	20030820	EP 2002-425075	20020213

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

PRIORITY APPLN. INFO.: EP 2002-425075 20020213
GI



II

AB New pharmaceutical compds. of general formula F-(X)q (I) [q = 1-5,

preferably 1; F is chosen among drugs such as δ-tocopherol, clidanac, diethylhomospermine, glucosamine, thymocartin, vofopitant, etc.; X is chosen among 4 groups M, T, V, and Y where M = ONO2, nitrate salt, nitrite ester, ONO, thoinitrite, SNO, etc., T = OR1-M, OR1OR1-M, SR1NR2R1-M, NR2R1-M, NR2R1SR1-M, etc., R1 = satd. or unsatd., linear or branched alkylene, having 1 to 21 carbon atoms or a satd. or unsatd., optionally heterosubstituted or branched cycloalkylene, having 3 to 7 carbon atoms or an optionally heterosubstituted arylene having 3 to 7 carbon atoms; R2 = H, satd. or unsatd., linear or branched 1-21 carbon atom alkyl, satd. or unsatd. optionally heterosubstituted or branched 3-7 carbon cycloalkyl, optionally heterosubstituted 3-7 carbon aryl; R1, R2 = OH, SH, F, Cl, Br, OPO3H2, CO2H, etc.; bond between F and T = carboxylic ester, carboxylic amide, glycoside, azo, thioester, sulfonic ester, etc.; V = Z-M2, OZ-M2, NR2Z-M2, R1Z-M2, OR1-M2, OR1Z-M2, M2 = M, R1-M, OR1-M, SR1-M, NR2R1-M; ZM2 = COCH2CH(M2)CH2N+Me3, COCH2CH2COM2, COCH(NHR2)CH2M2, etc.; Y = 4-COC6H4CH2ONO2, O(CH2)4ONO2, COCH(NH2)CH2ONO2, 3-OC6H4CH2ONO2, etc.] were prepd. For example, α-tocopherol reacted with 4-HO2CC6H4CH2ONO2 to give the nitroxymethyl deriv. II. The compds. of general formula I are nitrate prodrugs which can release nitric oxide in vivo in a controlled and selective way and without hypotensive side effects and for this reason they are useful for the prepn. of medicines for prevention and treatment of inflammatory, ischemic, degenerative and proliferative diseases of musculoskeletal, tegumental, respiratory, gastrointestinal, genito-urinary and central nervous systems.

IT **586347-55-9P**

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)

(prepn. of nitrate prodrugs for treating or preventing inflammatory, ischemic, degenerative, and proliferative diseases)

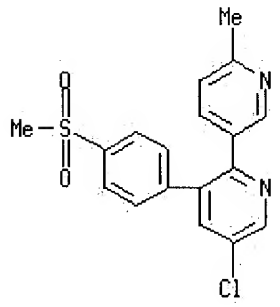
RN 586347-55-9 HCAPLUS

CN 2,3'-Bipyridine, 5-chloro-6'-methyl-3-[4-(methylsulfonyl)phenyl]-, nitrate (9CI) (CA INDEX NAME)

CM 1

CRN 202409-33-4

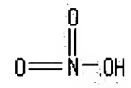
CMF C18 H15 Cl N2 O2 S



CM 2

CRN 7697-37-2

CMF H N O3



REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 2 OF 18 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2002:778724 HCAPLUS
DOCUMENT NUMBER: 137:284388
TITLE: 5-Chloro-3-(4-methanesulfonylphenyl)-6'-methyl-[2,3]bipyridinyl in pure crystalline form and process for synthesis
INVENTOR(S): Crocker, Loius S.; Davies, Ian W.; Osifchin, Richard G.; Kotliar, Andrew
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 13 pp., Cont.-in-part of U.S. Ser. No. 865,771.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002147221	A1	20021010	US 2001-957966	20010921
US 2002016343	A1	20020207	US 2001-865771	20010525
US 6521642	B2	20030218		
WO 2002096877	A1	20021205	WO 2001-US29551	20010921
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1395562	A1	20040310	EP 2001-973314	20010921
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 2003153600	A1	20030814	US 2003-342380	20030114
US 6673935	B2	20040106		

PRIORITY APPLN. INFO.:

US 2000-208017P	P	20000526
US 2001-865771	A2	20010525
WO 2001-US29551	W	20010921

AB This invention encompasses a pharmaceutical compn. comprising 5-chloro-3-(4-methanesulfonylphenyl)-6'-methyl-[2,3]bipyridinyl (I) in combination with a pharmaceutically acceptable carrier. The compd. I is comprised of about 1-50%, 1-20% or 1-10% of the polymorphic form which is designated Form V and the remainder of the compd. being comprised of at least one polymorphic form selected from the group consisting of Form I, Form II, Form III and Form IV. The compn. is useful as a selective inhibitor of cyclooxygenase-2 and as a non-steroidal anti-inflammatory agent.

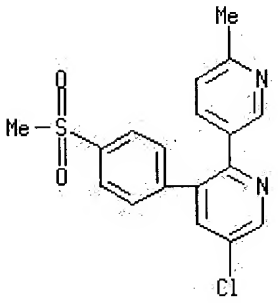
IT **287930-71-6P**
RL: CPS (Chemical process); PEP (Physical, engineering or chemical process); RCT (Reactant); **PREP (Preparation)**; **PREP**

(Preparation); PROC (Process); RACT (Reactant or reagent)
(compns. contg. polymorphic forms of bipyridinyl deriv. as COX-2 inhibitor and anti-inflammatory agent)

RN 287930-71-6 HCAPLUS
CN 2,3'-Bipyridine, 5-chloro-6'-methyl-3-[4-(methylsulfonyl)phenyl]-, mono(4-methylbenzenesulfonate) (9CI) (CA INDEX NAME)

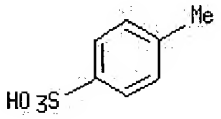
CM 1

CRN 202409-33-4
CMF C18 H15 Cl N2 O2 S



CM 2

CRN 104-15-4
CMF C7 H8 O3 S



L6 ANSWER 3 OF 18 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

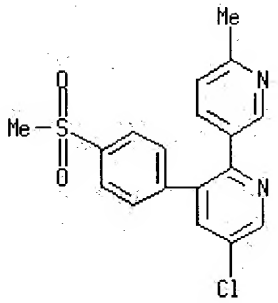
ACCESSION NUMBER: 2002:434902 HCAPLUS
DOCUMENT NUMBER: 137:210102
TITLE: Development of a derivatization method, coupled with reverse phase HPLC, for monitoring the formation of an enolate intermediate
AUTHOR(S): Abrahim, A.; Hartman, R.; Ge, Z.; Mao, B.; Marcoux, J.
CORPORATE SOURCE: Merck Research Laboratories, Rahway, NJ, 07065-0914, USA
SOURCE: Journal of Liquid Chromatography & Related Technologies (2002), 25(7), 1049-1062
CODEN: JLCTFC; ISSN: 1082-6076
PUBLISHER: Marcel Dekker, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A sensitive liq. chromatog. method was developed to monitor the formation of an enolate intermediate in a synthetic route to Etoricoxib, a drug candidate for the treatment of arthritis. The method requires the derivatization of the enolate with Me iodide to form a stable methylketosulfone deriv. followed by reverse phase HPLC anal. Parameters affecting the derivatization, including the nature of derivatizing agent, reaction solvent, amt. of derivatizing agent, reaction time, reaction

temp., and amt. of excess base in the reaction were studied. The derivatization reaction gave selective C-alkylation. The linear range of the chromatog. method for the detn. of the starting material, ketosulfone, and the deriv., methylketosulfone, was detd. Finally, the accuracy of the method was established based on recovery expts.

IT **202409-33-4P**, Etoricoxib
RL: PNU (Preparation, unclassified); **PREP (Preparation)**
(development of a derivatization method, coupled with reverse phase HPLC, for monitoring the formation of an enolate intermediate)

RN 202409-33-4 HCAPLUS
CN 2,3'-Bipyridine, 5-chloro-6'-methyl-3-[4-(methylsulfonyl)phenyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 4 OF 18 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2002:276519 HCAPLUS
DOCUMENT NUMBER: 136:310188
TITLE: Treatment of cancer with a prostate specific antigen (PSA) conjugate and an NSAID compound
INVENTOR(S): Heimbrook, David C.; Yao, Siu-long
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 129 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002042375	A1	20020411	US 2001-896245	20010629

PRIORITY APPLN. INFO.: US 2000-216217P P 20000705
OTHER SOURCE(S): MARPAT 136:310188

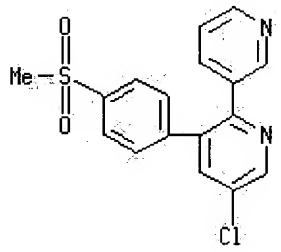
AB The invention relates to methods of treating cancer using a combination of a compd. which is a PSA conjugate and a nonsteroidal antiinflammatory agent (NSAID) and to methods of prepg. such compns. The PSA conjugate comprises an oligopeptide that is selectively cleaved by PSA and a cytotoxic agent. An example of a PSA conjugate is N-Ac-(4-trans-L-Hyp)-Ala-Ser-Chg-Gln-Ser-Leu-Dox (Dox = doxorubicin, Hyp = hydroxyproline, Chg = cyclohexylglycine) and COX-2 inhibitor 3-phenyl-4-[4-(4-methylsulfonyl)phenyl]-2(5H)furanone is an example of an NSAID compd. (syntheses given).

IT **202409-31-2P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**;

USES (Uses)
(treatment of cancer with prostate specific antigen (PSA) conjugate and NSAID compd.)

RN 202409-31-2 HCAPLUS

CN 2,3'-Bipyridine, 5-chloro-3-[4-(methylsulfonyl)phenyl]- (9CI) (CA INDEX NAME)



L6 ANSWER 5 OF 18 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2001:886073 HCAPLUS
DOCUMENT NUMBER: 136:11103
TITLE: 5-chloro-3-(4-methanesulfonylphenyl)-6'-methyl-[2,3']bipyridinyl in pure crystalline form and process for synthesis
INVENTOR(S): Crocker, Louis S.; Davies, Ian W.; Osifchin, Richard G.; Kotliar, Andrew
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 27 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001092230	A1	20011206	WO 2001-US16566	20010522
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1296951	A1	20030402	EP 2001-939267	20010522
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004501116	T2	20040115	JP 2002-500844	20010522
BG 107237	A	20030530	BG 2002-107237	20021031

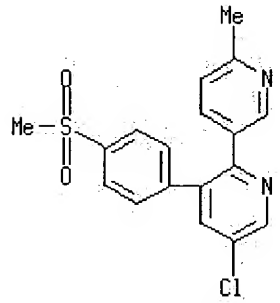
PRIORITY APPLN. INFO.: US 2000-208017P P 20000526
WO 2001-US16566 W 20010522

AB This invention encompasses the form V polymorph of the title compn. which is useful in the treatment of cyclooxygenase-2 mediated diseases. The invention encompasses certain pharmaceutical compns. for treatment of cyclooxygenase-2 mediated diseases comprising the Form V polymorph of the title compn. The invention also encompasses a process for synthesizing

the form V polymorph of the title compn. A mixt. of the title compn. and iso-Pr acetate was heated at 55°, then was cooled to ambient temp. and the solids were isolated by filtration. The solids were washed with iso-Pr acetate and dried in vacuo to give the form V polymorph as a colorless solid in about 87% yield.

IT **202409-33-4P**
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(methanesulfonylphenylmethyl bipyridinyl in pure cryst. form and process for synthesis)

RN 202409-33-4 HCAPLUS
CN 2,3'-Bipyridine, 5-chloro-6'-methyl-3-[4-(methylsulfonyl)phenyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 6 OF 18 HCAPLUS COPYRIGHT 2004 ACS on STN

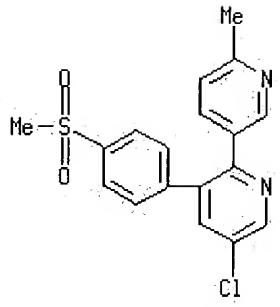
Full Text | Citing References

ACCESSION NUMBER: 2001:513717 HCAPLUS
DOCUMENT NUMBER: 136:95336
TITLE: Etoricoxib. Analgesic drug, antiarthritic, cyclooxygenase-2 inhibitor
AUTHOR(S): Sorbera, L. A.; Castaner, R. M.; Silvestre, J.; Castaner, J.
CORPORATE SOURCE: Prous Science, Barcelona, 08080, Spain
SOURCE: Drugs of the Future (2001), 26(4), 346-353
CODEN: DRFUD4; ISSN: 0377-8282
PUBLISHER: Prous Science
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with refs. describes the synthesis, pharmacol. studies, pharmacokinetics, and clin. studies of etoricoxib.

IT **202409-33-4P**, Etoricoxib
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(etoricoxib. analgesic drug, antiarthritic, cyclooxygenase-2 inhibitor)

RN 202409-33-4 HCAPLUS
CN 2,3'-Bipyridine, 5-chloro-6'-methyl-3-[4-(methylsulfonyl)phenyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 7 OF 18 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2001:396668 HCAPLUS
DOCUMENT NUMBER: 135:10027
TITLE: Polymorphic, amorphous and hydrated forms of 5-chloro-6'-methyl-3-[4-(methylsulfonyl)phenyl]-2,3'-bipyridine
INVENTOR(S): Clas, Sophie Dorothee; O'shea, Paul; Dalton, Chad; Crocker, Louis S.; Mccauley, James A.; Tillyer, Richard D.; Davies, Ian
PATENT ASSIGNEE(S): Merck Frosst Canada & Co., Can.
SOURCE: PCT Int. Appl., 20 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001037833	A1	20010531	WO 2000-US32353	20001127
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1248618	A1	20021016	EP 2000-980817	20001127
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003514859	T2	20030422	JP 2001-539448	20001127
US 6441002	B1	20020827	US 2000-724522	20001128
US 2002198238	A1	20021226	US 2002-180399	20020626
US 2003144327	A1	20030731	US 2003-342379	20030114

PRIORITY APPLN. INFO.:

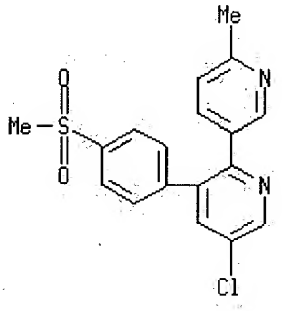
US 1999-167922P	P	19991129
WO 2000-US32353	W	20001127
US 2000-724522	A3	20001128
US 2002-180399	B1	20020626

AB Polymorphic, amorphous and hydrated forms of the title compd. having the following structure: are disclosed. The compd. is a potent and selective cyclooxygenase-2 inhibitor. The hemihydrate form of compd. A was produced by stirring Form IV in water for at least 1 day. XRPD anal. of the solid produced a diffractogram identical to the previous hemihydrate samples

obtained for Form II. Thermogravimetry confirmed that Form IV had converted to the hemihydrate form, exhibiting a sharp wt. loss of 2.45% on heating, which corresponds to a mole ratio of water to drug of 0.50%.

IT **340985-63-9P**
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(polymorphic and amorphous and hydrated forms of chloromethyl(methylsulfonyl)phenylbipyridine)

RN 340985-63-9 HCAPLUS
CN 2,3'-Bipyridine, 5-chloro-6'-methyl-3-[4-(methylsulfonyl)phenyl]-, hydrate (2:1) (9CI) (CA INDEX NAME)



1/2 H_2O

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 8 OF 18 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

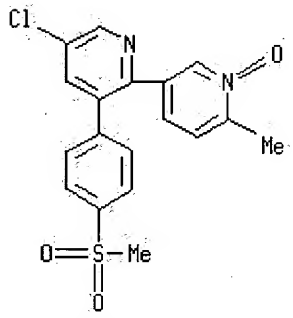
ACCESSION NUMBER: 2001:279045 HCAPLUS
DOCUMENT NUMBER: 135:86523
TITLE: In vitro metabolism considerations, including activity testing of metabolites, in the discovery and selection of the COX-2 inhibitor etoricoxib (MK-0663)
AUTHOR(S): Chauret, N.; Yergey, J. A.; Brideau, C.; Friesen, R. W.; Mancini, J.; Riendeau, D.; Silva, J.; Styhler, A.; Trimble, L. A.; Nicoll-Griffith, D. A.
CORPORATE SOURCE: Merck Frosst Centre for Therapeutic Research, Pointe-Claire-Dorval, QC, H9R 4P8, Can.
SOURCE: Bioorganic & Medicinal Chemistry Letters (2001), 11(8), 1059-1062
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Characterization of the metabolites of the COX-2 inhibitor etoricoxib (MK-0663 and L-791,456) produced in vitro indicate formation of an N-oxide pyridine and hydroxymethyl pyridine that can further be glucuronidated or oxidized to an acid. Significant turnover is obsd. in human hepatocytes. Several CYPs are involved in the oxidative biotranformations and, from in vitro studies, etoricoxib is not a potent CYP3A4 inducer or inhibitor. Based on an in vitro whole blood assay, none of the metabolites of etoricoxib inhibits COX-1 or contributes significantly to the inhibition of COX-2. Metabolites of the COX-2 inhibitor etoricoxib (MK-0663, L-791,456) produced in vitro are an N-oxide pyridine and hydroxymethyl pyridine that can further be glucuronidated or oxidized to an acid. In

vitro studies predicted no major metabolic liabilities in human. Based on an in vitro whole blood assay, none of the metabolites of etoricoxib inhibits COX-1 or contributes significantly to the inhibition of COX-2.

IT **325855-74-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); MFM (Metabolic formation); SPN (Synthetic preparation); BIOL (Biological study); FORM (Formation, nonpreparative);
PREP (Preparation)
(etoricoxib metabolite identification and their COX-2 inhibitory activity)

RN 325855-74-1 HCAPLUS
CN 2,3'-Bipyridine, 5-chloro-6'-methyl-3-[4-(methylsulfonyl)phenyl]-, 1'-oxide (9CI) (CA INDEX NAME)

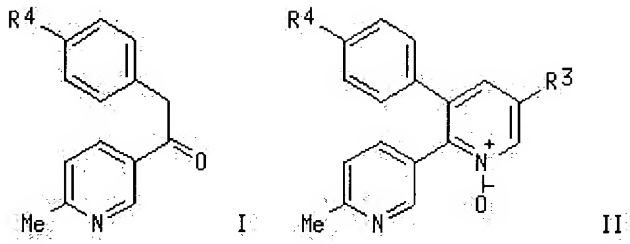


REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 9 OF 18 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2000:897114 HCAPLUS
DOCUMENT NUMBER: 134:178439
TITLE: A general [3 + 2 + 1] annulation strategy for the preparation of pyridine N-oxides
AUTHOR(S): Davies, Ian W.; Marcoux, Jean-Francois; Reider, Paul J.
CORPORATE SOURCE: Department of Process Research, Merck & Co. Inc., Rahway, NJ, 07065, USA
SOURCE: Organic Letters (2001), 3(2), 209-211
CODEN: ORLEF7; ISSN: 1523-7060
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 134:178439
GI



AB Stabilized ketone, aldehyde, and ester enolates, generated from I (R4 = MeSO2, MeS) for example, react with vinamidinium hexafluorophosphate salts

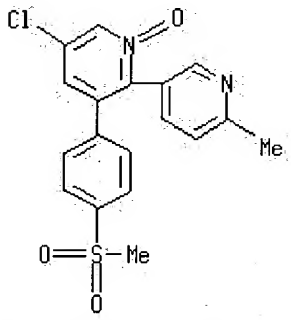
and hydroxylamine hydrochloride to give pyridine N-oxides, e.g. II (R3 = Cl, NO2), in 45-85% yields.

IT **325855-71-8P**

RL: SPN (Synthetic preparation); **PREP (Preparation)**
(prepn. of pyridine N-oxides by cyclization of vinamidinium salts with enolates of ketones, aldehydes, and esters)

RN 325855-71-8 HCAPLUS

CN 2,3'-Bipyridine, 5-chloro-6'-methyl-3-[4-(methylsulfonyl)phenyl]-, 1-oxide (9CI) (CA INDEX NAME)



REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 10 OF 18 HCAPLUS COPYRIGHT 2004 ACS on STN

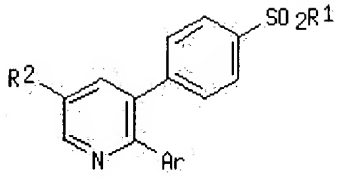
Full Text | Citing References

ACCESSION NUMBER: 2000:699219 HCAPLUS
DOCUMENT NUMBER: 133:266735
TITLE: Preparation of 2,3-diaryl-5-halopyridines from halomalondialdehydes, benzyl aryl ketones, and ammonium reagents.
INVENTOR(S): Pye, Philip J.; Rossen, Kai; Maliakal, Ashok; Volante, Ralph P.; Sager, Jess; Marcoux, Jean-francois; Davies, Ian; Corley, Edward G.; Sidler, Daniel Richard; Larsen, Robert D.
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: U.S., 12 pp., Cont.-in-part of U.S. Ser. No. 60,731.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6127545	A	20001003	US 1998-156846	19980918
US 6130334	A	20001010	US 1998-60731	19980415
AU 753381	B2	20021017	AU 2001-38932	20010427

PRIORITY APPLN. INFO.: US 1997-45642P P 19970418
US 1998-60731 A2 19980415

OTHER SOURCE(S): CASREACT 133:266735; MARPAT 133:266735
GI



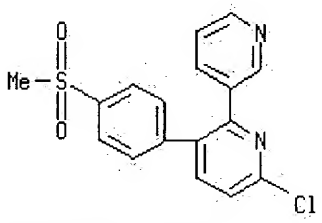
I

AB Title compds. [I; R1 = Me, NH2, NHCOCF3, NHMe; Ar = (substituted) Ph, pyridinyl; R2 = F, Cl, Br, iodo, cyano], were prepd. by reaction of HOCH:CR2CHO with 4-(R1SO2)C6H4CH2COAr (variables as above) and an ammonium reagent under acidic conditions. Thus, HOCH:CClCHO (prepn. given), 4-methylsulfonylbenzyl 3-pyridyl ketone (prepn. given), and NH4OAc were heated at 130° with distn. of HOAc of reaction to give 55% 5-chloro-3-(4-methylsulfonylphenyl)-2-(3-pyridyl)pyridine.

IT **221615-70-9P**, 5-Chloro-3-(4-methylsulfonylphenyl)-2-(3-pyridyl)pyridine
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); **PREP (Preparation)**
(prepn. of 2,3-diaryl-5-halopyridines from halomalondialdehydes, benzyl aryl ketones, and ammonium reagents)

RN 221615-70-9 HCAPLUS

CN 2,3'-Bipyridine, 6-chloro-3-[4-(methylsulfonyl)phenyl]- (9CI) (CA INDEX NAME)

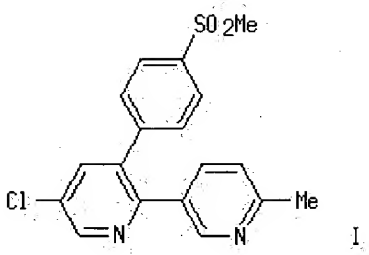


REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 11 OF 18 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2000:653182 HCAPLUS
DOCUMENT NUMBER: 134:4838
TITLE: A Practical Synthesis of a COX-2-Specific Inhibitor
AUTHOR(S): Davies, Ian W.; Marcoux, Jean-Francois; Corley, Edward G.; Journet, Michel; Cai, Dong-Wei; Palucki, Michael; Wu, Jimmy; Larsen, Robert D.; Rossen, Kai; Pye, Philip J.; DiMichele, Lisa; Dormer, Peter; Reider, Paul J.
CORPORATE SOURCE: Department of Process Research, Merck Co. Inc., Rahway, NJ, 07065, USA
SOURCE: Journal of Organic Chemistry (2000), 65(25), 8415-8420
CODEN: JOCEAH; ISSN: 0022-3263
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 134:4838
GI



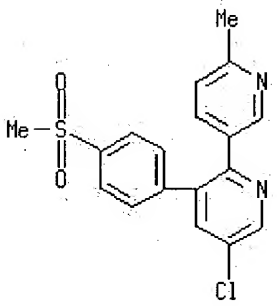
I

AB A no. of synthetic strategies to the Cox-2 specific inhibitor have been described. These studies have led to the identification of a novel pyridine construction using annulation of a ketone using a vinamidinium species and ammonia in 97% assay yield. Three approaches to the synthesis of the ketone are described that allow for its prepn. in large quantities in >65% overall yield from Me 6-methylnicotinate.

IT **202409-33-4P**
RL: SPN (Synthetic preparation); **PREP (Preparation)**
(prepn. of a methylsulfonylphenylbipyridine COX-2 inhibitor)

RN 202409-33-4 HCAPLUS

CN 2,3'-Bipyridine, 5-chloro-6'-methyl-3-[4-(methylsulfonyl)phenyl]- (9CI) (CA INDEX NAME)

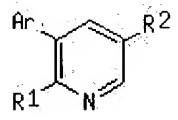


REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

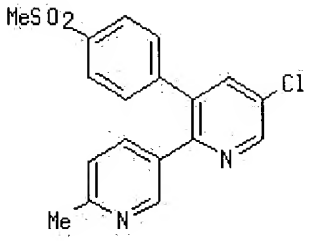
L6 ANSWER 12 OF 18 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2000:443023 HCAPLUS
DOCUMENT NUMBER: 133:222553
TITLE: Annulation of Ketones with Vinamidinium Hexafluorophosphate Salts: An Efficient Preparation of Trisubstituted Pyridines
AUTHOR(S): Marcoux, Jean-Francois; Corley, Edward G.; Rossen, Kai; Pye, Phil; Wu, Jimmy; Robbins, Michael A.; Davies, Ian W.; Larsen, Robert D.; Reider, Paul J.
CORPORATE SOURCE: Department of Process Research, Merck Co. Inc., Rahway, NJ, 07065, USA
SOURCE: Organic Letters (2000), 2(15), 2339-2341
CODEN: ORLEF7; ISSN: 1523-7060
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 133:222553
GI



I



II

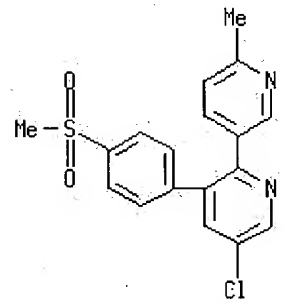
AB α-Aryl ketones react with vinamidinium hexafluorophosphate salts to give access to the corresponding 3-arylpyridines I (Ar = C6H4R-4, R = SO2Me, H, SMe, R1 = 6-methyl-3-pyridyl, C6H4R-4, R2 = Cl; Ar = C6H4SO2Me-4, R1 = 6-methyl-3-pyridyl, R2 = Br, I, CF3, NO2, phthalimido; Ar = C6H4F-4, R1 = Me, R2 = Cl; Ar = Ph, R1 = H, R2 = Cl). The annulation reactions proceed in good to excellent yields with vinamidinium salts contg. electron-withdrawing groups at the β-position (R2). The reaction was applied to the prepn. of the COX-2 specific inhibitor 5-chloro-3-(4-methylsulfonyl)phenyl-2-(2-methyl-5-pyridinyl)pyridine (II), as well as a series of analogs.

IT **202409-33-4P**

RL: SPN (Synthetic preparation); **PREP (Preparation)**
(prepn. of trisubstituted pyridines via annulation of ketones with vinamidinium hexafluorophosphate salts)

RN 202409-33-4 HCAPLUS

CN 2,3'-Bipyridine, 5-chloro-6'-methyl-3-[4-(methylsulfonyl)phenyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 13 OF 18 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1999:708874 HCAPLUS
DOCUMENT NUMBER: 131:322542
TITLE: Process for synthesizing arylpyridine COX-2 inhibitors
INVENTOR(S): Corley, Edward G.; Davies, Ian W.; Larsen, Robert D.; Pye, Philip J.; Rossen, Kai
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

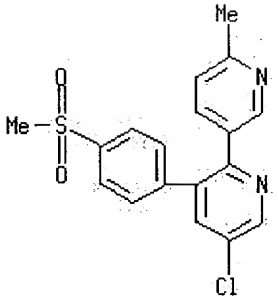
```
     WO 9955830         A2   19991104       WO 1999-US8645   19990420
     WO 9955830         A3   19991229
         W:  AE, AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GD,
             GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV,
             MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM,
             TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK,
             ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG,
             CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     CA 2329193         AA   19991104       CA 1999-2329193  19990420
     EP 1071745         A2   20010131       EP 1999-918706   19990420
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE,
             SI, LT, LV, FI, RO
     BR 9909844         A    20010403       BR 1999-9844     19990420
     JP 3325264         B2   20020917       JP 2000-545976   19990420
     AU 759469          B2   20030417       AU 1999-36557    19990420
     CZ 292515          B6   20031015       CZ 2000-3940     19990420
     NZ 507597          A    20040227       NZ 1999-507597   19990420
     US 6040319         A    20000321       US 1999-298127   19990423
     TW 474934          B    20020201       TW 1999-88106545 19990423
     US 6252116         B1   20010626       US 2000-488774   20000121
     HR 2000000722      A1   20010630       HR 2000-722      20001024
PRIORITY APPLN. INFO.:                  US 1998-82888P   P   19980424
                                        US 1998-85668P   P   19980515
                                        WO 1999-US8645   W   19990420
                                        US 1999-298127   A3  19990423
OTHER SOURCE(S):        CASREACT 131:322542; MARPAT 131:322542
GI
```

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention encompasses a process and intermediates for prepg. compds. I [R, R', R'' = (un)substituted alkyl, aryl, aralkyl, halo, SOmH, SOm-alkyl, SOm-aryl, NO2, (di)(alkyl)amino, SOmNH2, SOmNH-alkyl, SOmNHCOCF3, cyano; Y = C, N; m = 0, 1, 2]. I are useful in the treatment of cyclooxygenase-2 mediated diseases (no data), i.e., as analgesics, antipyretics, and antiinflammatories. The method comprises cyclocondensation of an iminium salt II [R2-R5 = alkyl, aryl, or aralkyl; X- = suitable counterion] with an aryl ketone III in the presence of a base. The method is designed to give high yields at low temps., and with a reduced no. of steps. For instance, the bipyridyl deriv. IV was prepd. on a 1.65-kg scale by reaction of the iminium salt V with ketone VI in THF in the presence of KOBu-tert, followed by quenching in AcOH/THF, basification with concd. aq. NH4OH, and refluxing. Prepns. of the salt and ketone intermediates V and VI are described, and a subset of the iminium salt intermediates II are claimed per se.

IT **202409-33-4P**, 5-Chloro-6'-methyl-3-[4-(methylsulfonyl)phenyl]-2,3'-bipyridine
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); **PREP (Preparation)**
(target compd.; prepn. of arylpyridine COX-2 inhibitors by cyclocondensation of iminium salts with ketones)

RN 202409-33-4 HCAPLUS
CN 2,3'-Bipyridine, 5-chloro-6'-methyl-3-[4-(methylsulfonyl)phenyl]- (9CI) (CA INDEX NAME)



L6 ANSWER 14 OF 18 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1999:282039 HCAPLUS
DOCUMENT NUMBER: 130:306593
TITLE: Combination therapy using a HMG-CoA reductase inhibitor and a cyclooxygenase-2 (COX-2) inhibitor for reducing the risks associated with cardio- and cerebrovascular disease
INVENTOR(S): Winokur, Melvin
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 55 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9920110	A1	19990429	WO 1998-US21901	19981016
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GD, GE, HR, HU, ID, IL, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2306646	AA	19990429	CA 1998-2306646	19981016
AU 9913612	A1	19990510	AU 1999-13612	19981016
AU 753657	B2	20021024		
EP 1024696	A1	20000809	EP 1998-957328	19981016
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO				
JP 2001520174	T2	20011030	JP 2000-516533	19981016
US 6245797	B1	20010612	US 1998-179349	19981020

PRIORITY APPLN. INFO.:

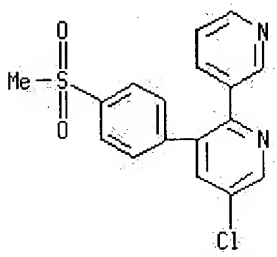
US 1997-62691P	P	19971022
GB 1998-6688	A	19980327
WO 1998-US21901	W	19981016

AB The invention provides a drug combination comprised of a HMG-CoA reductase inhibitor in combination with a COX-2 inhibitor, which is useful for treating, preventing, and/or reducing the risk of developing atherosclerosis and atherosclerotic disease events. Prepn. of selected COX-2 inhibitors, e.g. 5-chloro-3-(4-methylsulfonyl)phenyl-2-(2-methyl-5-pyridinyl)pyridine, is described. Pharmaceutical formulations are included.

IT **202409-31-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);

BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(HMG-CoA reductase inhibitor combination with COX-2 inhibitor for reducing risks assocd. with cardio- and cerebrovascular disease, COX-2 inhibitor prepn., and pharmaceutical formulations)

RN 202409-31-2 HCAPLUS
CN 2,3'-Bipyridine, 5-chloro-3-[4-(methylsulfonyl)phenyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 15 OF 18 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1999:222917 HCAPLUS
DOCUMENT NUMBER: 130:252250
TITLE: Preparation of 3-phenyl-2-(3-pyridyl)pyridines and intermediates.
INVENTOR(S): Davies, Ian W.; Gerena, Linda; Journet, Michel; Larsen, Robert D.; Pye, Philip J.; Rossen, Kai
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 42 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9915503	A2	19990401	WO 1998-US19788	19980922
WO 9915503	A3	19990520		
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GD, GE, HR, HU, ID, IL, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6040450	A	20000321	US 1998-153405	19980915
AU 9895002	A1	19990412	AU 1998-95002	19980922
EP 1023266	A2	20000802	EP 1998-948426	19980922
EP 1023266	B1	20030108		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
BR 9812837	A	20000808	BR 1998-12837	19980922
JP 2001517654	T2	20011009	JP 2000-512812	19980922
JP 3325263	B2	20020917		
AT 230726	E	20030115	AT 1998-948426	19980922
ES 2189251	T3	20030701	ES 1998-948426	19980922
CN 1134414	B	20040114	CN 1998-811147	19980922

SK 283811	B6	20040203	SK 2000-422		19980922
US 6204387	B1	20010320	US 2000-509230		20000323
US 6369275	B1	20020409	US 2000-715736		20001117
HK 1029343	A1	20030502	HK 2001-100155		20010106
PRIORITY APPLN. INFO.:			US 1997-60680P	P	19970925
			GB 1998-6419	A	19980325
			WO 1998-US19788	W	19980922
			US 2000-509230	A3	20000323

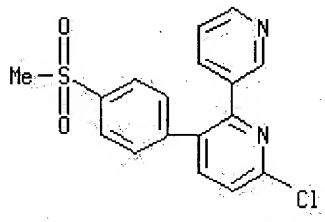
OTHER SOURCE(S): CASREACT 130:252250; MARPAT 130:252250

AB P-(ArCOCH2)C6H4SO2R1 (R1 = Me, NH2, NHCOCF3, NHMe; Ar = mono-, di-, or trisubstituted Ph, pyridyl, N-oxide thereof), were prepd. by reaction of p-MeSC6H4CH2MgX (X = Cl, Br, F, iodo) with ArCONMe2 (Ar as above) to give p-(ArCOCH2)C6H4SMe followed by oxidn. of the latter. Thus, the Grignard reagent from p-MeSC6H4CH2Cl in PhMe/THF was added to a -20° soln. of 6-methylnicotinic acid N-methyl-N-methoxyamide (prepn. given) in PhMe over 30 min. followed by 1 h aging to give 76% 2-methyl-5-(4-methylthiophenylacetyl)pyridine. The latter in MeOH/H2SO4 at 55° was treated with aq. Na tungstate and then with H2O2 over 1 h to give 82.5% 2-methyl-5-(4-methylsulfonylphenylacetyl)pyridine. The latter reacted with 3-amino-2-chloroacrolein (prepn. given) to give 65% 5-chloro-2-(2-methylpyrid-5-yl)-3-(4-methylsulfonylphenyl)pyridine.

IT **221615-70-9P**, 5-Chloro-3-(4-methylsulfonylphenyl)-2-(3-pyridyl)pyridine
RL: SPN (Synthetic preparation); **PREP (Preparation)**
(prepn. of 3-phenyl-2-(3-pyridyl)pyridines and intermediates)

RN 221615-70-9 HCAPLUS

CN 2,3'-Bipyridine, 6-chloro-3-[4-(methylsulfonyl)phenyl]- (9CI) (CA INDEX NAME)

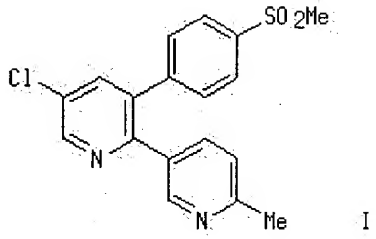


L6 ANSWER 16 OF 18 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER:	1998:710173 HCAPLUS
DOCUMENT NUMBER:	130:52303
TITLE:	2-Pyridinyl-3-[4-(methylsulfonyl)phenyl]pyridines: selective and orally active cyclooxygenase-2 inhibitors
AUTHOR(S):	Friesen, Richard W.; Brideau, Christine; Chan, Chi Chung; Charleson, Stella; Deschenes, Denis; Dube, Daniel; Ethier, Diane; Fortin, Rejean; Gauthier, Jacques Yves; Girard, Yves; Gordon, Robert; Greig, Gillian M.; Riendeau, Denis; Savoie, Chantal; Wang, Zhaoyin; Wong, Elizabeth; Visco, Denise; Xu, Li Jing; Young, Robert N.
CORPORATE SOURCE:	Merck Frosst Centre for Therapeutic Research, Pointe Claire-Dorval, QC, H9R 4P8, Can.
SOURCE:	Bioorganic & Medicinal Chemistry Letters (1998), 8(19), 2777-2782 CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER:	Elsevier Science Ltd.

DOCUMENT TYPE: Journal
LANGUAGE: English
GI

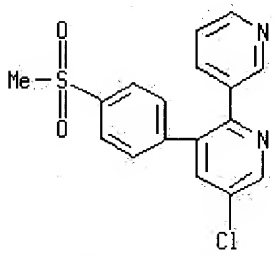


I

AB The title compds. were prepd. and evaluated for their ability to inhibit the isoenzymes of cyclooxygenase, COX-1 and COX-2. Optimum COX-2 activity was obsd. by introduction of a substituent at C5 of the central pyridine. Pyridine deriv. I was identified as the optimum compd. in this series.

IT **202409-31-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); **PREP (Preparation)**
(2-pyridinyl-3-[4-(methylsulfonyl)phenyl]pyridines as cyclooxygenase-2 inhibitors)

RN 202409-31-2 HCAPLUS
CN 2,3'-Bipyridine, 5-chloro-3-[4-(methylsulfonyl)phenyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 17 OF 18 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1998:709052 HCAPLUS
DOCUMENT NUMBER: 129:316152
TITLE: Preparation of 2-aryl-3-aryl-5-halo pyridines as cyclooxygenase-2 (COX-2) inhibitors
INVENTOR(S): Pye, Philip J.; Maliakal, Ashok; Rossen, Kai; Volante, Ralph P.; Sager, Jess
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

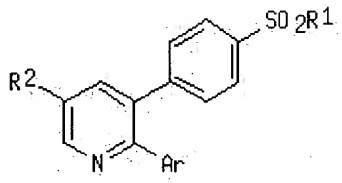
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 9847871	A1	19981029	WO 1998-US8312	19980414
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, GW, HU, ID, IL, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
TW 492959	B	20020701	TW 1998-87105349	19980409
AU 9872571	A1	19981113	AU 1998-72571	19980414
AU 729730	B2	20010208		
EP 975596	A1	20000202	EP 1998-919881	19980414
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, FI, RO				
BR 9808923	A	20000801	BR 1998-8923	19980414
JP 2000513018	T2	20001003	JP 1998-546367	19980414
JP 3300369	B2	20020708		
NZ 500390	A	20010831	NZ 1998-500390	19980414
CZ 293246	B6	20040317	CZ 1999-3690	19980414
HR 980206	B1	20020228	HR 1998-980206	19980416
MX 9909584	A	20000331	MX 1999-9584	19991018
AU 753381	B2	20021017	AU 2001-38932	20010427

PRIORITY APPLN. INFO.:	US 1997-45642P	P	19970418
	GB 1997-9686	A	19970513
	WO 1998-US8312	W	19980414

OTHER SOURCE(S): MARPAT 129:316152

GI



I

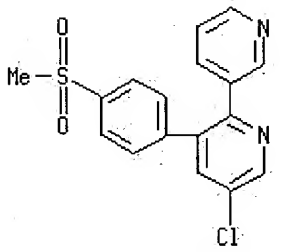
AB The title compds. [I; Ar = mono-, di- or trisubstituted Ph, pyridinyl or pyridinyl N-oxide; R1 = Me, NH2, NHCOCF3 NHMe; R2 = F, Cl, Br, iodo, cyano, azido] which inhibit COX-2 in synthesis of prostaglandin E2 in the presence of arachidonic acid with IC50 of 1 nM - 1 mM (no exptl. details) and are useful in the treatment of inflammations and COX-2 mediated diseases, were prepd., e.g., by cyclocondensation of benzyl ketones 4-R1O2SC6H4CH2COAr (Ar, R1 as above) with aldehydes HOCH:CR2CHO (R2 as above) under acidic conditions, in the presence of an ammonium reagent. For example, acylation of MeSC6H4 with ClCOCO2Et and sapon. of the ester gave 4-MeSC6H4COCO2H which was subjected (without isolation) to Wolff-Kishner redn. to give 4-MeSC6H4CH2CO2H. This was oxidized with H2O2 in H2O in the presence of Na2WO4·2H2O and Aliquat 336 to give 4-MeSO2C6H4CH2CO2H which was converted to Grignard compd. with Me3CMgCl and condensed with Et nicotinate to give 4-(methylsulfonyl)benzyl 3-pyridyl ketone. Heating of the latter with HOCH:CClCHO and NH4OAc at 130° gave the title compd. I (Ar = 3-pyridyl, R1 = Me, R2 = Cl).

IT **202409-31-2P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(prepn. of 2-aryl-3-aryl-5-halo pyridines as cyclooxygenase-2 inhibitors)

RN 202409-31-2 HCAPLUS

CN 2,3'-Bipyridine, 5-chloro-3-[4-(methylsulfonyl)phenyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 18 OF 18 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1998:87712 HCAPLUS
DOCUMENT NUMBER: 128:140614
TITLE: Preparation of substituted pyridines as selective cyclooxygenase-2 inhibitors
INVENTOR(S): Dube, Daniel; Fortin, Rejean; Friesen, Richard; Wang, Zhaoyin; Gauthier, Jacques Yves
PATENT ASSIGNEE(S): Merck Frosst Canada Inc., Can.; Dube, Daniel; Fortin, Rejean; Friesen, Richard; Wang, Zhaoyin; Gauthier, Jacques Yves
SOURCE: PCT Int. Appl., 88 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9803484	A1	19980129	WO 1997-CA486	19970708
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, HU, IL, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2260016	AA	19980129	CA 1997-2260016	19970708
CA 2412968	AA	19980129	CA 1997-2412968	19970708
AU 9733319	A1	19980210	AU 1997-33319	19970708
AU 723179	B2	20000817		
EP 912518	A1	19990506	EP 1997-929067	19970708
EP 912518	B1	20030910		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO				
CN 1225085	A	19990804	CN 1997-196377	19970708
BR 9710372	A	19990817	BR 1997-10372	19970708
JP 11514008	T2	19991130	JP 1997-506397	19970708
NZ 333230	A	20000825	NZ 1997-333230	19970708
JP 3251945	B2	20020128	JP 1998-506397	19970708
JP 2002080453	A2	20020319	JP 2001-209904	19970708
EE 3680	B1	20020415	EE 1999-18	19970708

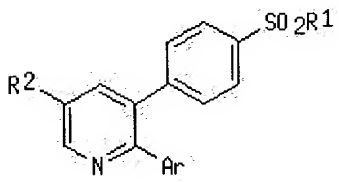
IL 127441	A1	20030212	IL 1997-127441	19970708
SK 283261	B6	20030401	SK 1999-36	19970708
AT 249437	E	20030915	AT 1997-929067	19970708
CZ 292843	B6	20031217	CZ 1999-130	19970708
PT 912518	T	20031231	PT 1997-929067	19970708
US 5861419	A	19990119	US 1997-893395	19970711
TW 453994	B	20010911	TW 1997-86110013	19970715
ZA 9706335	A	19980318	ZA 1997-6335	19970717
HR 970389	B1	20021031	HR 1997-970389	19970717
US 6001843	A	19991214	US 1998-181887	19981029
NO 9900191	A	19990316	NO 1999-191	19990115
US 6071936	A	20000606	US 1999-312790	19990517
US 2003065011	A1	20030403	US 2001-21187	20011030
US 6596736	B2	20030722		
US 2004029921	A1	20040212	US 2003-395788	20030324

PRIORITY APPLN. INFO.:

US 1996-22128P	P	19960718
GB 1996-16126	A	19960801
US 1996-27139P	P	19961001
GB 1996-21420	A	19961015
US 1997-41814P	P	19970408
GB 1997-9291	A	19970507
CA 1997-2260016	A3	19970708
JP 1998-506397	A3	19970708
WO 1997-CA486	W	19970708
US 1997-893395	A3	19970711
US 1998-181887	A3	19981029
US 1999-312790	A1	19990517
US 2000-570191	A3	20000515
US 2001-21187	A3	20011030

OTHER SOURCE(S): MARPAT 128:140614

GI



I

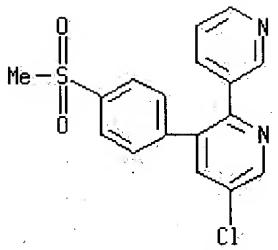
AB The title compds. [I; R1 = Me, NH2, NHC(O)CF3, NHMe; Ar = (un)substituted Ph, pyridyl (or the N-oxide thereof); R2 = halo, C1-6 alkoxy, C1-6 alkylthio, etc.], useful for treating antiinflammatory diseases comprising, were prepd. Thus, reaction of 2-bromo-3-(4-methylsulfonyl)phenyl-5-trifluoromethylpyridine with di-Et 3-pyridylborane in the presence of PdBr2(PPh3)2 and Na2CO3 in PhH/EtOH afforded I [R1 = Me; R2 = CF3; Ar = 3-pyridyl] which showed IC50 of 1.8 μM against COX-2 (whole blood) vs. IC50 of 5 μM against COX-1 (U937).

IT **202409-31-2P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); **PREP (Preparation)**; **PREP (Preparation)**; RACT (Reactant or reagent); USES (Uses)
(prepn. of substituted pyridines as selective cyclooxygenase-2 inhibitors)

RN 202409-31-2 HCAPLUS

CN 2,3'-Bipyridine, 5-chloro-3-[4-(methylsulfonyl)phenyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> **file reg**

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	87.98	257.77

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-12.47	-12.47

FILE 'REGISTRY' ENTERED AT 16:36:44 ON 07 MAY 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 5 MAY 2004 HIGHEST RN 680179-46-8
DICTIONARY FILE UPDATES: 5 MAY 2004 HIGHEST RN 680179-46-8

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2004

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=>
L8 STRUCTURE UPLOADED

=> **d l8**
L8 HAS NO ANSWERS
L8 STR

H 28 C [illegible] O [illegible] N M2 F 32

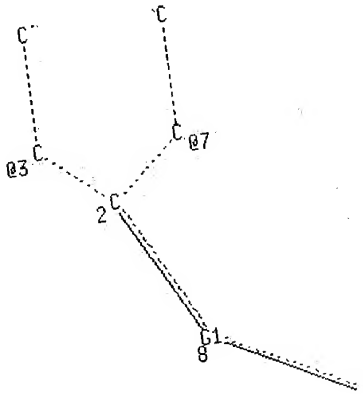
O 26 S 27

N @1

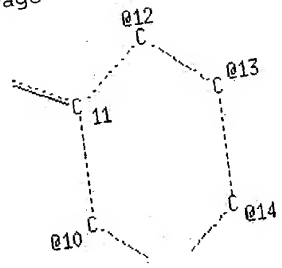
Page 1-C

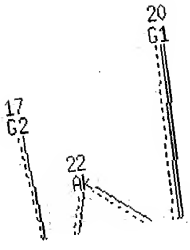
Ak 23

Page 2-A



Page 2-C

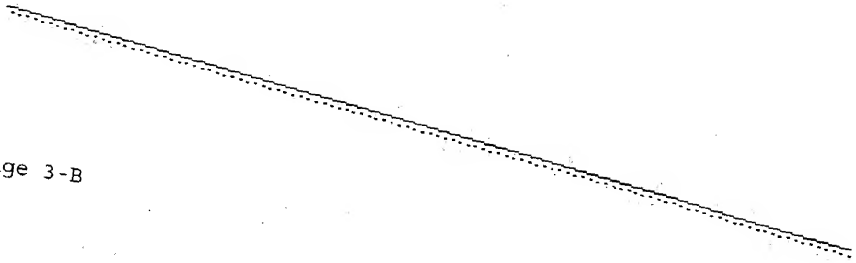




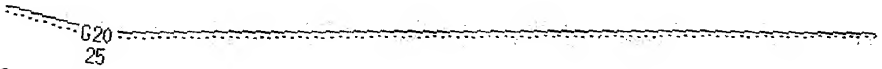
Page 2-D

24 Cu

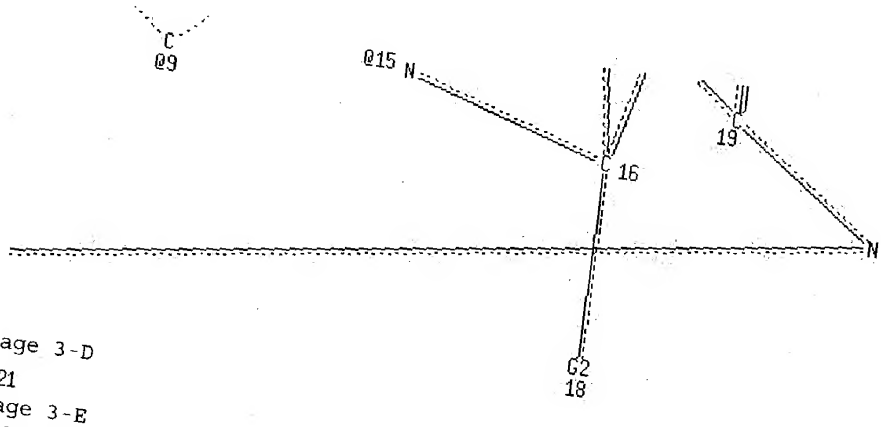
Page 3-A



Page 3-B



Page 3-C



Page 3-D

21

Page 3-E

```
VAR G1=26/27
VAR G2=28/29/30/31/32
REP G20=(0-1) 23-21 23-24
VPA 15-9/10/12/13/14 S
VPA 1-3/4/5/6/7 S
NODE ATTRIBUTES:
HCOUNT   IS M3      AT  29
HCOUNT   IS M1      AT  30
HCOUNT   IS M2      AT  31
NSPEC    IS C       AT   1
NSPEC    IS R       AT   2
NSPEC    IS R       AT   3
NSPEC    IS R       AT   4
NSPEC    IS R       AT   5
NSPEC    IS R       AT   6
NSPEC    IS C       AT   7
NSPEC    IS R       AT   8
NSPEC    IS R       AT   9
NSPEC    IS R       AT  10
NSPEC    IS R       AT  11
NSPEC    IS R       AT  12
NSPEC    IS R       AT  13
NSPEC    IS C       AT  14
NSPEC    IS C       AT  15
NSPEC    IS C       AT  16
NSPEC    IS C       AT  17
NSPEC    IS C       AT  18
NSPEC    IS C       AT  19
NSPEC    IS C       AT  20
```

```
NSPEC   IS C      AT  21
NSPEC   IS C      AT  22
NSPEC   IS C      AT  23
NSPEC   IS C      AT  24
NSPEC   IS C      AT  25
DEFAULT MLEVEL IS ATOM
MLEVEL  IS CLASS  AT   1 15 16 19 21 22 23 26 27 28 29 30 31 32
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC I
NUMBER OF NODES IS  32

STEREO ATTRIBUTES: NONE


=> s l8
SAMPLE SEARCH INITIATED 16:37:41 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -   3915 TO ITERATE

 25.5% PROCESSED    1000 ITERATIONS                                  0 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:        74549 TO    82051
PROJECTED ANSWERS:             0 TO        0

L9             0 SEA SSS SAM L8

=> s l8 full
THE ESTIMATED SEARCH COST FOR FILE 'REGISTRY' IS 155.00 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N or END:y
FULL SEARCH INITIATED 16:37:46 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -  78240 TO ITERATE

100.0% PROCESSED   78240 ITERATIONS                                 2 ANSWERS
SEARCH TIME: 00.00.03

L10            2 SEA SSS FUL L8

=> file hcaplus
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                    155.84     413.61

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                       ENTRY    SESSION
CA SUBSCRIBER PRICE                                      0.00     -12.47

FILE 'HCAPLUS' ENTERED AT 16:37:52 ON 07 MAY 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)


Copyright of the articles to which records in this database refer is
held by the publishers listed in the PUBLISHER (PB) field (available
for records published or updated in Chemical Abstracts after December
```

FILE COVERS 1907 - 7 May 2004 VOL 140 ISS 20
FILE LAST UPDATED: 6 May 2004 (20040506/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> **s l10**
L11 1 L10

=> **d l11, ibib abs fhitstr, 1**

L11 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1987:578176 HCAPLUS
DOCUMENT NUMBER: 107:178176
TITLE: Use of aromatic amines for setting epoxide resins
INVENTOR(S): Nichols, Gus
PATENT ASSIGNEE(S): USA
SOURCE: U.S., 9 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

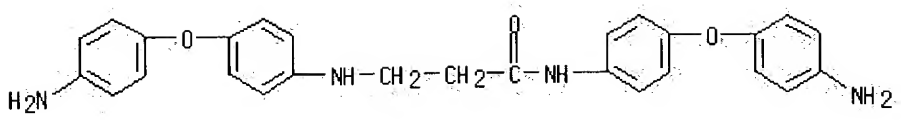
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4668757	A	19870526	US 1984-593592	19840326

PRIORITY APPLN. INFO.: US 1984-593592 19840326

AB Arom. amines and their alkyl, imine, amide, and/or imide group-contg. derivs. are used with epoxy resins and catalysts comprising phenols, cresols, etc., in the prepn. of compns. which cure at ambient temps. The compns. are useful as 2-component coating or casting systems. Condensing 2.0 mol 2,4-bis(p-aminobenzyl)aniline with 3.0 mol phthalic anhydride to remove 3.0 mol H2O gave an imide-amine, which (47 g) was mixed with 28 g iso-BuCOMe and 25 g toluene to give a soln. The soln. was mixed an equal amt. of a soln. comprising Epon 828 51.3, o-cresol 5, toluene 12, and iso-BuCOMe 31.7 g to give a coating compn. which had pot life 1.5 h and gave coatings which were tackfree after 3 h and hard after 12 h. Without o-cresol, the films remained tacky for weeks.

IT **110712-35-1D**, reaction products with tetraethylene glycol diacrylate and hydroxypropyl acrylate
RL: USES (Uses)
(curing by, of epoxy resins in presence of phenol catalysts)

RN 110712-35-1 HCAPLUS
CN Propanamide, N-[4-(4-aminophenoxy)phenyl]-3-[[4-(4-aminophenoxy)phenyl]amino]- (9CI) (CA INDEX NAME)



```
=> file reg
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     7.12     420.73

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                       ENTRY    SESSION
CA SUBSCRIBER PRICE                                    -0.69     -13.16

FILE 'REGISTRY' ENTERED AT 16:38:05 ON 07 MAY 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2004 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:     5 MAY 2004  HIGHEST RN 680179-46-8
DICTIONARY FILE UPDATES:    5 MAY 2004  HIGHEST RN 680179-46-8

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2004

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=> d his

     (FILE 'HOME' ENTERED AT 16:33:18 ON 07 MAY 2004)

     FILE 'REGISTRY' ENTERED AT 16:33:55 ON 07 MAY 2004

     FILE 'USPATFULL' ENTERED AT 16:34:01 ON 07 MAY 2004
L1            94 S NICHOLS, G?/AU
L2             6 S L1 AND EPOXIDE?

     FILE 'REGISTRY' ENTERED AT 16:35:18 ON 07 MAY 2004
L3               STRUCTURE UPLOADED
L4            30 S L3 FULL

     FILE 'HCAPLUS' ENTERED AT 16:36:03 ON 07 MAY 2004
L5           176 S L4
L6            18 S L4/PREP
L7             0 S L6 AND GUS, N?/AU

     FILE 'REGISTRY' ENTERED AT 16:36:44 ON 07 MAY 2004
L8               STRUCTURE UPLOADED
L9             0 S L8
```

```
L10             2 S L8 FULL

     FILE 'HCAPLUS' ENTERED AT 16:37:52 ON 07 MAY 2004
L11             1 S L10

     FILE 'REGISTRY' ENTERED AT 16:38:05 ON 07 MAY 2004

=> s l10/prep
'PREP' IS NOT A VALID CROSSOVER QUALIFIER FOR L10
Answer sets created in a different file may be field qualified with a
limited set of qualifiers.  Enter HELP CROSSOVER at an arrow prompt
(=>) for specific information.

=> file hcaplus
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     0.42     421.15

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                       ENTRY    SESSION
CA SUBSCRIBER PRICE                                     0.00     -13.16

FILE 'HCAPLUS' ENTERED AT 16:38:15 ON 07 MAY 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)


Copyright of the articles to which records in this database refer is
held by the publishers listed in the PUBLISHER (PB) field (available
for records published or updated in Chemical Abstracts after December
26, 1996), unless otherwise indicated in the original publications.
The CA Lexicon is the copyrighted intellectual property of the
the American Chemical Society and is provided to assist you in searching
databases on STN.  Any dissemination, distribution, copying, or storing
of this information, without the prior written consent of CAS, is
strictly prohibited.

FILE COVERS 1907 - 7 May 2004  VOL 140 ISS 20
FILE LAST UPDATED: 6 May 2004  (20040506/ED)

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.


=> s l10/prep
             1 L10
       3144401 PREP/RL
L12          1 L10/PREP
                 (L10 (L) PREP/RL)

=> d l12, ibib abs hitstr, 1

L12  ANSWER 1 OF 1  HCAPLUS  COPYRIGHT 2004 ACS on STN
```


```
ACCESSION NUMBER:         1987:578176  HCAPLUS
DOCUMENT NUMBER:          107:178176
TITLE:                    Use of aromatic amines for setting epoxide resins
INVENTOR(S):              Nichols, Gus
```

PATENT ASSIGNEE(S): USA
SOURCE: U.S., 9 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

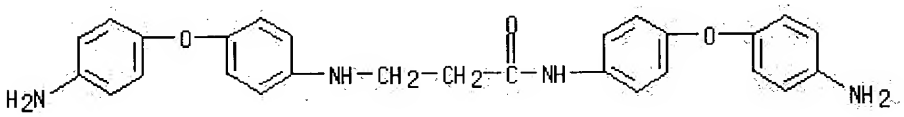
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4668757	A	19870526	US 1984-593592	19840326

PRIORITY APPLN. INFO.: US 1984-593592 19840326

AB Arom. amines and their alkyl, imine, amide, and/or imide group-contg. derivs. are used with epoxy resins and catalysts comprising phenols, cresols, etc., in the prepn. of compns. which cure at ambient temps. The compns. are useful as 2-component coating or casting systems. Condensing 2.0 mol 2,4-bis(p-aminobenzyl)aniline with 3.0 mol phthalic anhydride to remove 3.0 mol H2O gave an imide-amine, which (47 g) was mixed with 28 g iso-BuCOMe and 25 g toluene to give a soln. The soln. was mixed an equal amt. of a soln. comprising Epon 828 51.3, o-cresol 5, toluene 12, and iso-BuCOMe 31.7 g to give a coating compn. which had pot life 1.5 h and gave coatings which were tackfree after 3 h and hard after 12 h. Without o-cresol, the films remained tacky for weeks.

IT **110712-35-1P**
RL: **PREP (Preparation)**
(manuf. of, for curing of epoxy resins in presence of phenol catalysts)

RN 110712-35-1 HCAPLUS
CN Propanamide, N-[4-(4-aminophenoxy)phenyl]-3-[[4-(4-aminophenoxy)phenyl]amino]- (9CI) (CA INDEX NAME)



=> **file reg**

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	14.19	435.34
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-0.69	-13.85

FILE 'REGISTRY' ENTERED AT 16:40:26 ON 07 MAY 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 5 MAY 2004 HIGHEST RN 680179-46-8
DICTIONARY FILE UPDATES: 5 MAY 2004 HIGHEST RN 680179-46-8

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2004

Please note that search-term pricing does apply when

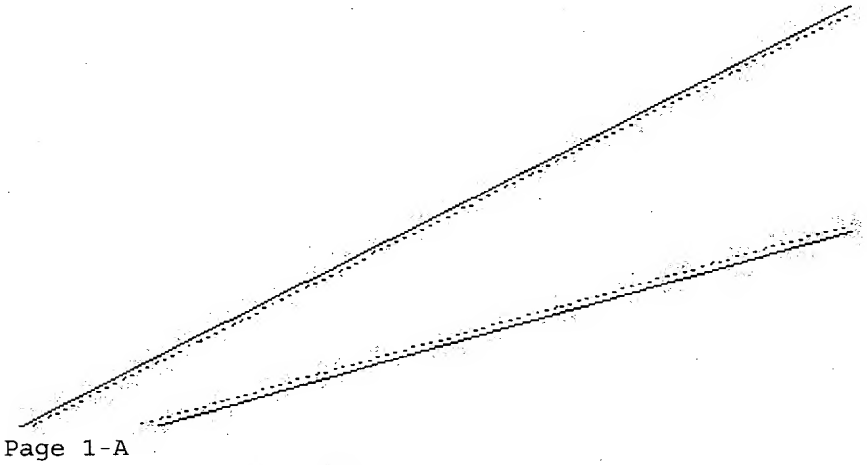
conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

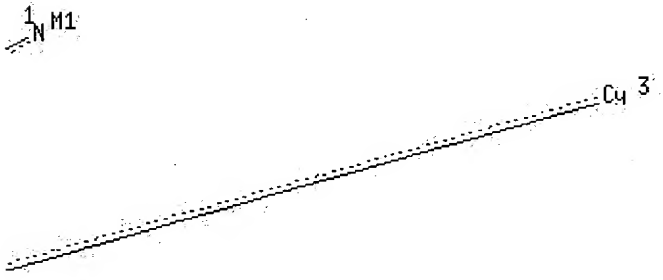
=>
L14 STRUCTURE UPLOADED

=> **d l14**
L14 HAS NO ANSWERS
L14 STR

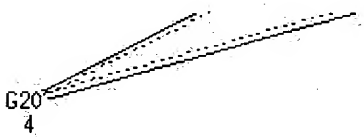


Page 1-A

Ak 2



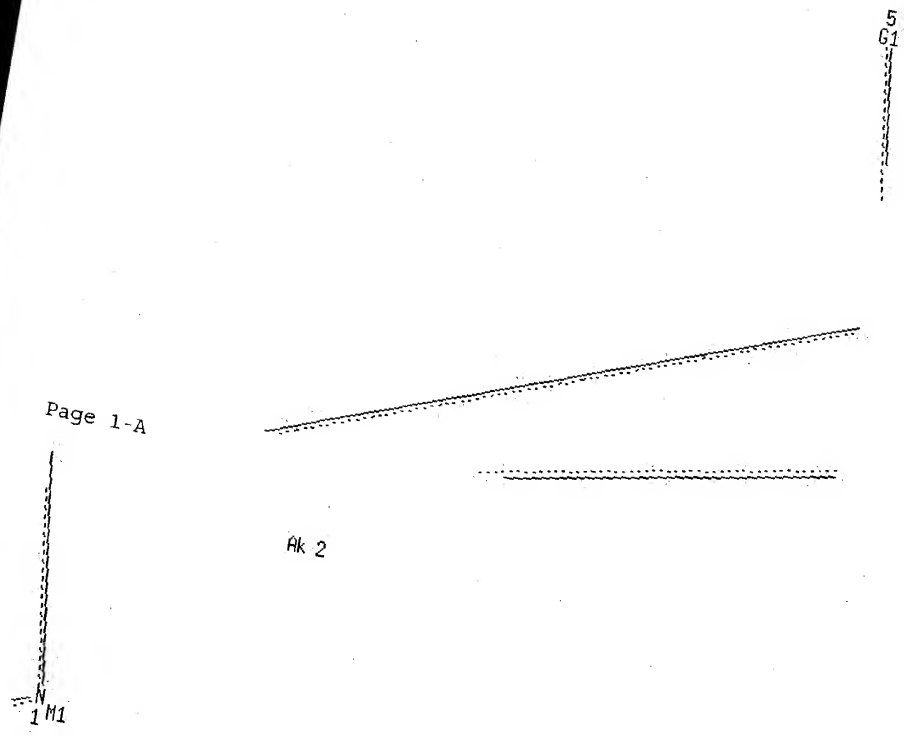
Page 1-B



Page 2-A
REP G20=(0-1) 2-1 2-3
NODE ATTRIBUTES:
HCOUNT IS M1 AT 1
NSPEC IS C AT 1
NSPEC IS C AT 2

```
NSPEC   IS C       AT   3
NSPEC   IS C       AT   4
DEFAULT MLEVEL IS ATOM
MLEVEL  IS CLASS   AT   1  2
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS   4

STEREO ATTRIBUTES: NONE


=> d his

     (FILE 'HOME' ENTERED AT 16:33:18 ON 07 MAY 2004)

     FILE 'REGISTRY' ENTERED AT 16:33:55 ON 07 MAY 2004

     FILE 'USPATFULL' ENTERED AT 16:34:01 ON 07 MAY 2004
L1            94 S NICHOLS, G?/AU
L2             6 S L1 AND EPOXIDE?

     FILE 'REGISTRY' ENTERED AT 16:35:18 ON 07 MAY 2004
L3               STRUCTURE UPLOADED
L4            30 S L3 FULL

     FILE 'HCAPLUS' ENTERED AT 16:36:03 ON 07 MAY 2004
L5           176 S L4
L6            18 S L4/PREP
L7             0 S L6 AND GUS, N?/AU

     FILE 'REGISTRY' ENTERED AT 16:36:44 ON 07 MAY 2004
L8               STRUCTURE UPLOADED
L9             0 S L8
L10            2 S L8 FULL

     FILE 'HCAPLUS' ENTERED AT 16:37:52 ON 07 MAY 2004
L11            1 S L10

     FILE 'REGISTRY' ENTERED AT 16:38:05 ON 07 MAY 2004

     FILE 'HCAPLUS' ENTERED AT 16:38:15 ON 07 MAY 2004
L12            1 S L10/PREP

     FILE 'REGISTRY' ENTERED AT 16:40:26 ON 07 MAY 2004
L13              STRUCTURE UPLOADED
L14              STRUCTURE UPLOADED

=> s l14
SAMPLE SEARCH INITIATED 16:42:38 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 809349 TO ITERATE

  0.1% PROCESSED    1000 ITERATIONS                          50 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.02

FULL FILE PROJECTIONS:  ONLINE  **INCOMPLETE**
                        BATCH   **INCOMPLETE**
PROJECTED ITERATIONS:      EXCEEDS 1000000
```

```
PROJECTED ANSWERS:
L15                    EXCEEDS 1000000
                50 SEA SSS SAM L14
=>
L16          STRUCTURE UPLOADED
=> d l16
L16 HAS NO ANSWERS
L16
Ak 6 H 7              STR
```




```
VAR G1=6/7
REP G20=(0-1) 2-1 2-3
```

```
NODE ATTRIBUTES:
HCOUNT  IS M1     AT   1
NSPEC   IS C      AT   1
NSPEC   IS C      AT   2
NSPEC   IS C      AT   3
NSPEC   IS C      AT   4
NSPEC   IS C      AT   5
DEFAULT MLEVEL IS ATOM
MLEVEL  IS CLASS  AT   1  2  6  7
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS   7

STEREO ATTRIBUTES: NONE


=> s l16
SAMPLE SEARCH INITIATED 16:43:56 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 809349 TO ITERATE

  0.1% PROCESSED    1000 ITERATIONS                                 50 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **INCOMPLETE**
                        BATCH   **INCOMPLETE**
PROJECTED ITERATIONS:      EXCEEDS 1000000
PROJECTED ANSWERS:         EXCEEDS 1000000

L17          50 SEA SSS SAM L16

=> d his

     (FILE 'HOME' ENTERED AT 16:33:18 ON 07 MAY 2004)

     FILE 'REGISTRY' ENTERED AT 16:33:55 ON 07 MAY 2004

     FILE 'USPATFULL' ENTERED AT 16:34:01 ON 07 MAY 2004
L1           94 S NICHOLS, G?/AU
L2            6 S L1 AND EPOXIDE?

     FILE 'REGISTRY' ENTERED AT 16:35:18 ON 07 MAY 2004
L3               STRUCTURE UPLOADED
L4           30 S L3 FULL

     FILE 'HCAPLUS' ENTERED AT 16:36:03 ON 07 MAY 2004
L5          176 S L4
L6           18 S L4/PREP
L7            0 S L6 AND GUS, N?/AU

     FILE 'REGISTRY' ENTERED AT 16:36:44 ON 07 MAY 2004
L8               STRUCTURE UPLOADED
L9            0 S L8
L10           2 S L8 FULL

     FILE 'HCAPLUS' ENTERED AT 16:37:52 ON 07 MAY 2004
L11           1 S L10
```

```
     FILE 'REGISTRY' ENTERED AT 16:38:05 ON 07 MAY 2004

     FILE 'HCAPLUS' ENTERED AT 16:38:15 ON 07 MAY 2004
L12             1 S L10/PREP

     FILE 'REGISTRY' ENTERED AT 16:40:26 ON 07 MAY 2004
L13                STRUCTURE UPLOADED
L14                STRUCTURE UPLOADED
L15            50 S L14
L16                STRUCTURE UPLOADED
L17            50 S L16

=> file hcaplus
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                      ENTRY    SESSION
FULL ESTIMATED COST                                    2.52     437.86

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                      ENTRY    SESSION
CA SUBSCRIBER PRICE                                    0.00     -13.85

FILE 'HCAPLUS' ENTERED AT 16:44:09 ON 07 MAY 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)

Copyright of the articles to which records in this database refer is
held by the publishers listed in the PUBLISHER (PB) field (available
for records published or updated in Chemical Abstracts after December
26, 1996), unless otherwise indicated in the original publications.
The CA Lexicon is the copyrighted intellectual property of the
the American Chemical Society and is provided to assist you in searching
databases on STN.  Any dissemination, distribution, copying, or storing
of this information, without the prior written consent of CAS, is
strictly prohibited.

FILE COVERS 1907 - 7 May 2004  VOL 140 ISS 20
FILE LAST UPDATED: 6 May 2004  (20040506/ED)

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.


=> d his

     (FILE 'HOME' ENTERED AT 16:33:18 ON 07 MAY 2004)

     FILE 'REGISTRY' ENTERED AT 16:33:55 ON 07 MAY 2004

     FILE 'USPATFULL' ENTERED AT 16:34:01 ON 07 MAY 2004
L1             94 S NICHOLS, G?/AU
L2              6 S L1 AND EPOXIDE?

     FILE 'REGISTRY' ENTERED AT 16:35:18 ON 07 MAY 2004
L3                 STRUCTURE UPLOADED
L4             30 S L3 FULL

     FILE 'HCAPLUS' ENTERED AT 16:36:03 ON 07 MAY 2004
L5            176 S L4
```

```
L6            18 S L4/PREP
L7             0 S L6 AND GUS, N?/AU

     FILE 'REGISTRY' ENTERED AT 16:36:44 ON 07 MAY 2004
L8               STRUCTURE UPLOADED
L9             0 S L8
L10            2 S L8 FULL

     FILE 'HCAPLUS' ENTERED AT 16:37:52 ON 07 MAY 2004
L11            1 S L10

     FILE 'REGISTRY' ENTERED AT 16:38:05 ON 07 MAY 2004

     FILE 'HCAPLUS' ENTERED AT 16:38:15 ON 07 MAY 2004
L12            1 S L10/PREP

     FILE 'REGISTRY' ENTERED AT 16:40:26 ON 07 MAY 2004
L13              STRUCTURE UPLOADED
L14              STRUCTURE UPLOADED
L15           50 S L14
L16              STRUCTURE UPLOADED
L17           50 S L16

     FILE 'HCAPLUS' ENTERED AT 16:44:09 ON 07 MAY 2004

=> d l12, ibib abs hitstr, 1


L12  ANSWER 1 OF 1  HCAPLUS  COPYRIGHT 2004 ACS on STN
```

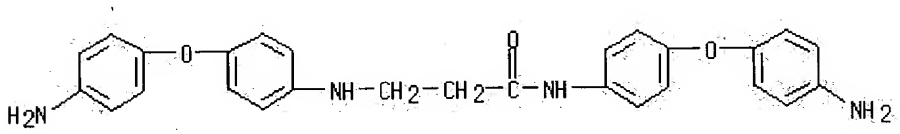
Full Text | Citing References

```
ACCESSION NUMBER:          1987:578176  HCAPLUS
DOCUMENT NUMBER:           107:178176
TITLE:                     Use of aromatic amines for setting epoxide resins
INVENTOR(S):               Nichols, Gus
PATENT ASSIGNEE(S):        USA
SOURCE:                    U.S., 9 pp.
                           CODEN: USXXAM
DOCUMENT TYPE:             Patent
LANGUAGE:                  English
FAMILY ACC. NUM. COUNT:    1
PATENT INFORMATION:

     PATENT NO.        KIND  DATE           APPLICATION NO.   DATE
     ----------------  ----  --------       ----------------  --------
     US 4668757         A    19870526       US 1984-593592    19840326
PRIORITY APPLN. INFO.:                     US 1984-593592      19840326
AB   Arom. amines and their alkyl, imine, amide, and/or imide group-contg.
     derivs. are used with epoxy resins and catalysts comprising phenols,
     cresols, etc., in the prepn. of compns. which cure at ambient temps.  The
     compns. are useful as 2-component coating or casting systems.  Condensing
     2.0 mol 2,4-bis(p-aminobenzyl)aniline with 3.0 mol phthalic anhydride to
     remove 3.0 mol H2O gave an imide-amine, which (47 g) was mixed with 28 g
     iso-BuCOMe and 25 g toluene to give a soln.  The soln. was mixed an equal
     amt. of a soln. comprising Epon 828 51.3, o-cresol 5, toluene 12, and
     iso-BuCOMe 31.7 g to give a coating compn. which had pot life 1.5 h and
     gave coatings which were tackfree after 3 h and hard after 12 h.  Without
     o-cresol, the films remained tacky for weeks.
IT 110712-35-1P
     RL: PREP (Preparation)
```

(manuf. of, for curing of epoxy resins in presence of phenol catalysts)

RN 110712-35-1 HCAPLUS

CN Propanamide, N-[4-(4-aminophenoxy)phenyl]-3-[[4-(4-aminophenoxy)phenyl]amino]- (9CI) (CA INDEX NAME)



=> **file reg**

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	73.18	511.04

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-0.69	-14.54

FILE 'REGISTRY' ENTERED AT 17:01:43 ON 07 MAY 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2004 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 6 MAY 2004 HIGHEST RN 680568-77-8
DICTIONARY FILE UPDATES: 6 MAY 2004 HIGHEST RN 680568-77-8

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2004

Please note that search-term pricing does apply when conducting SmartSELECT searches.

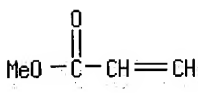
Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=> **e methyl acrylate/cn**

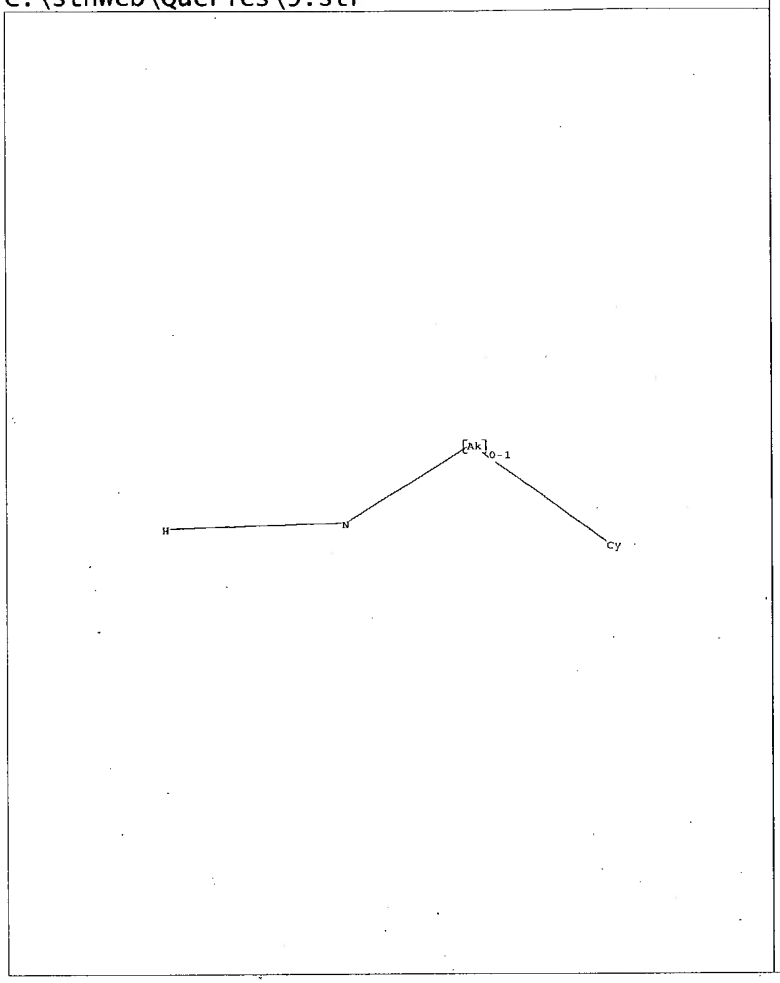
E1	1	METHYL ACRYLAMIDOGLYCOLATE METHYL ETHER HOMOPOLYMER/CN
E2	1	METHYL ACRYLAMIDOGLYCOLATE METHYL ETHER-VINYLPYRROLIDONE COPOLYMER/CN
E3	1 -->	METHYL ACRYLATE/CN
E4	1	METHYL ACRYLATE COMPOUND WITH METHYL LINOLATE (1:1)/CN
E5	1	METHYL ACRYLATE DIANION/CN
E6	1	METHYL ACRYLATE DIMER/CN
E7	1	METHYL ACRYLATE HOMOPOLYMER/CN
E8	1	METHYL ACRYLATE HOMOPOLYMER DOCOSYL ESTER/CN
E9	1	METHYL ACRYLATE HOMOPOLYMER DODECYL ESTER/CN
E10	1	METHYL ACRYLATE HOMOPOLYMER EICOSYL ESTER/CN
E11	1	METHYL ACRYLATE HOMOPOLYMER ESTER WITH 1-(2-HYDROXYETHYL) PYRROLIDINE/CN
E12	1	METHYL ACRYLATE HOMOPOLYMER ESTER WITH 2-(2-HYDROXYETHYL)PYRIDINE/CN

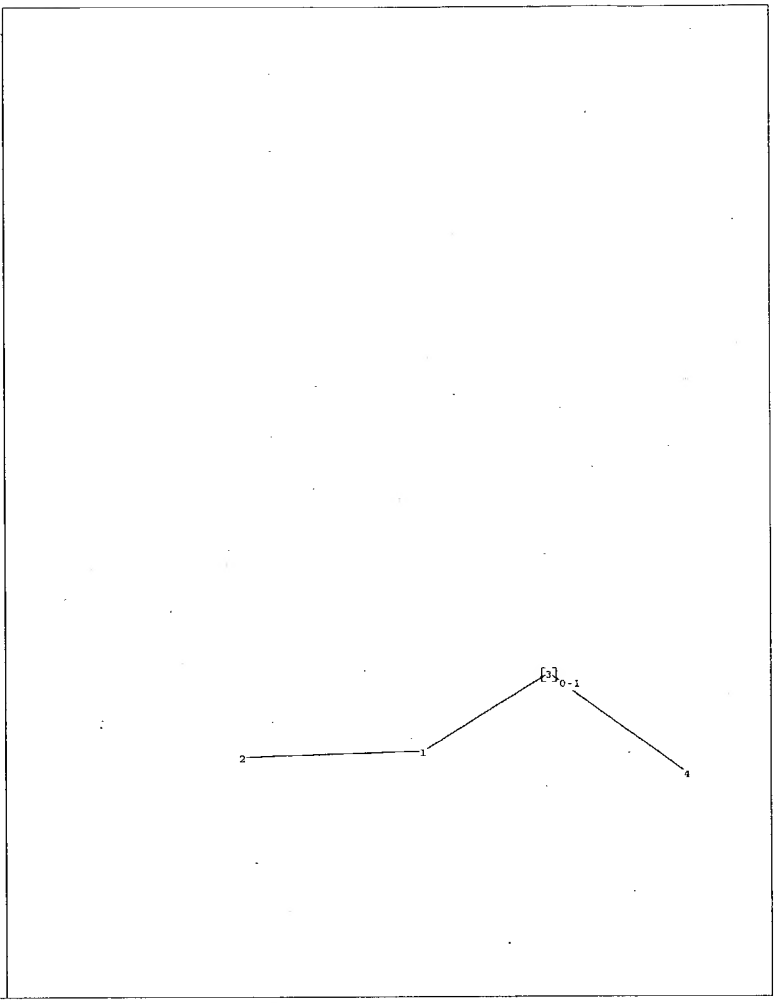
```
=> s e3
L18             1 "METHYL ACRYLATE"/CN

=> d l18

L18  ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2004 ACS on STN
RN   96-33-3  REGISTRY
CN   2-Propenoic acid, methyl ester (9CI)  (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN   Acrylic acid methyl ester (6CI, 8CI)
OTHER NAMES:
CN   2-Propenoic acid methyl ester
CN   Methoxycarbonylethylene
CN   Methyl acrylate
CN   Methyl acrylic ester
CN   Methyl prop-2-enoate
CN   Methyl propenoate
CN   NSC 24146
FS   3D CONCORD
DR   102256-29-1
MF   C4 H6 O2
CI   COM
LC   STN Files:   AGRICOLA, ANABSTR, AQUIRE, BEILSTEIN*, BIOBUSINESS, BIOSIS,
       BIOTECHNO, CA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS,
       CHEMINFORMRX, CHEMLIST, CHEMSAFE, CIN, CSCHEM, CSNB, DETHERM*, DIPPR*,
       EMBASE, ENCOMPLIT, ENCOMPLIT2, ENCOMPPAT, ENCOMPPAT2, GMELIN*, HODOC*,
       HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NIOSHTIC,
       PDLCOM*, PIRA, PROMT, PS, RTECS*, SPECINFO, SYNTHLINE, TOXCENTER, TULSA,
       ULIDAT, USPAT2, USPATFULL, VTB
         (*File contains numerically searchable property data)
     Other Sources:   DSL**, EINECS**, TSCA**
         (**Enter CHEMLIST File for up-to-date regulatory information)
```



```
**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

           12059 REFERENCES IN FILE CA (1907 TO DATE)
             870 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
           12073 REFERENCES IN FILE CAPLUS (1907 TO DATE)
             313 REFERENCES IN FILE CAOLD (PRIOR TO 1967)


=>
```

C:\stnweb\Queries\9.str

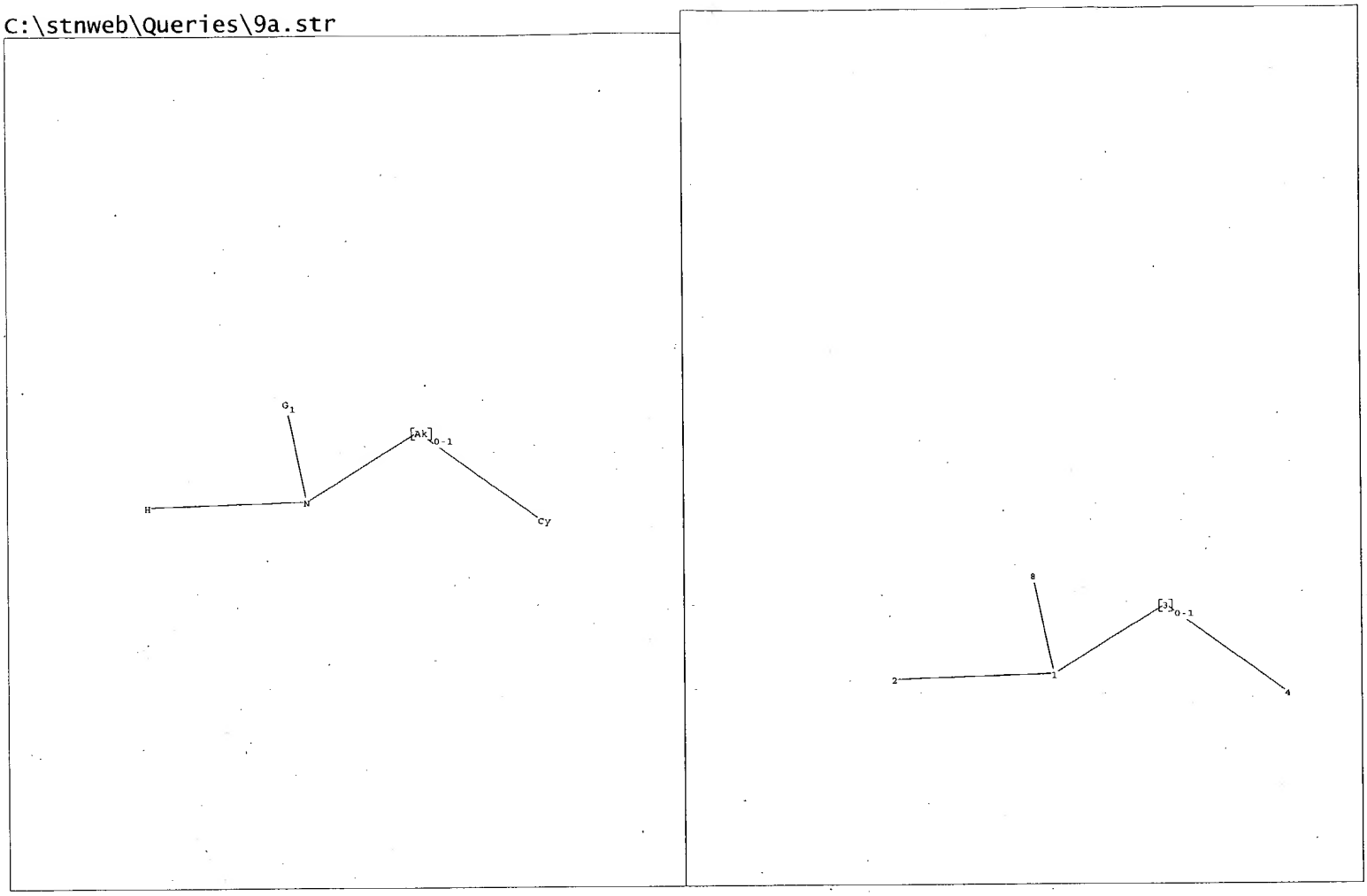




chain nodes :
1 2 3 4
chain bonds :
1-2 1-3 3-4
exact/norm bonds :
1-3 3-4
exact bonds :
1-2

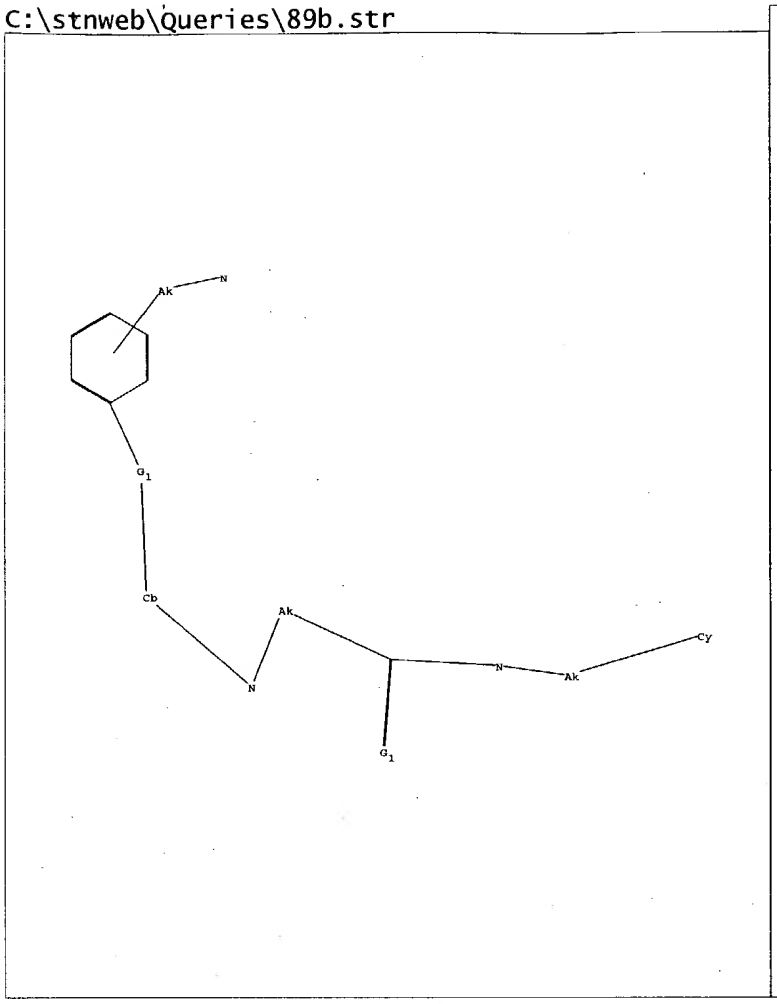
Match level :
1:CLASS 2:CLASS 3:CLASS 4:Atom

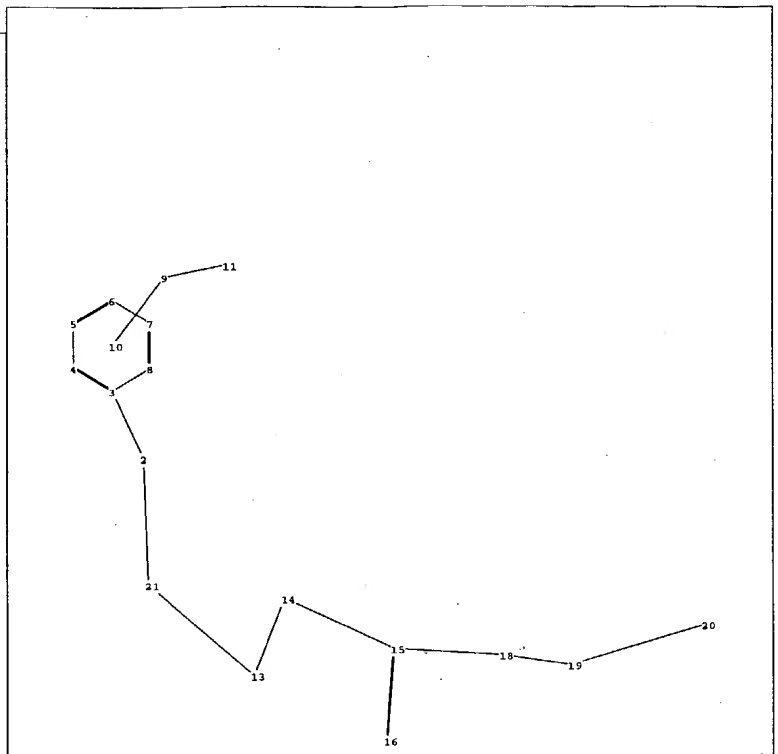
C:\stnweb\Queries\9a.str




```
chain nodes :
    1  2  3  4  8
chain bonds :
    1-2  1-3  1-8  3-4
exact/norm bonds :
    1-3  1-8  3-4
exact bonds :
    1-2


G1:Ak,H

Match level :
    1:CLASS  2:CLASS  3:CLASS  4:Atom  8:CLASS
```

C:\stnweb\Queries\89b.str



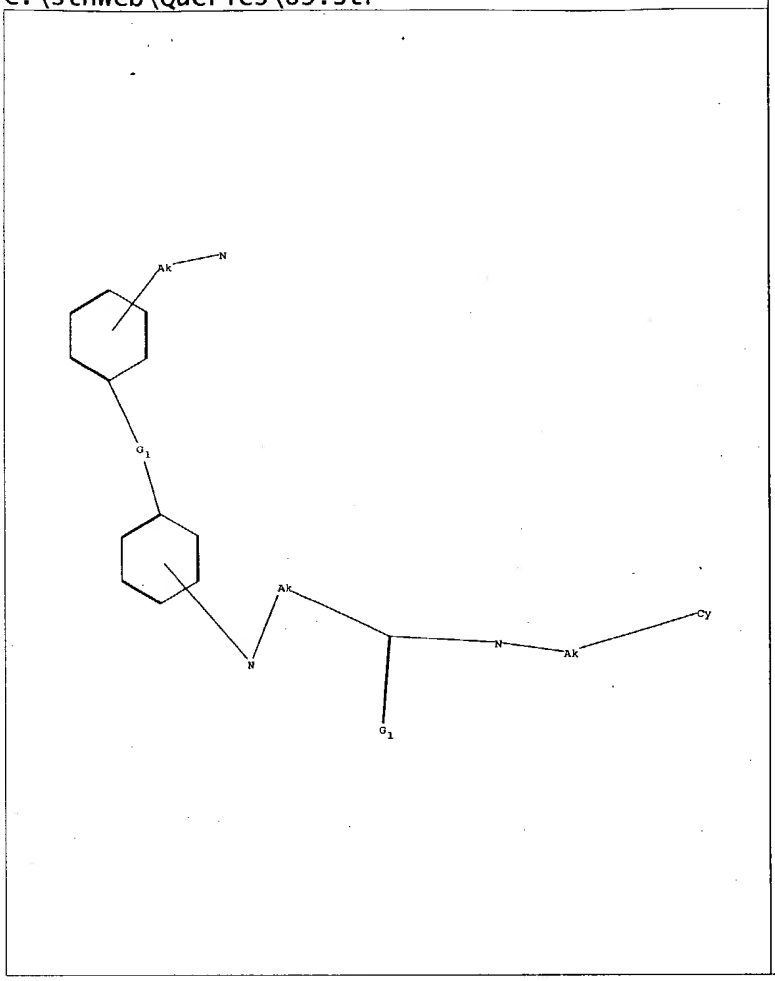


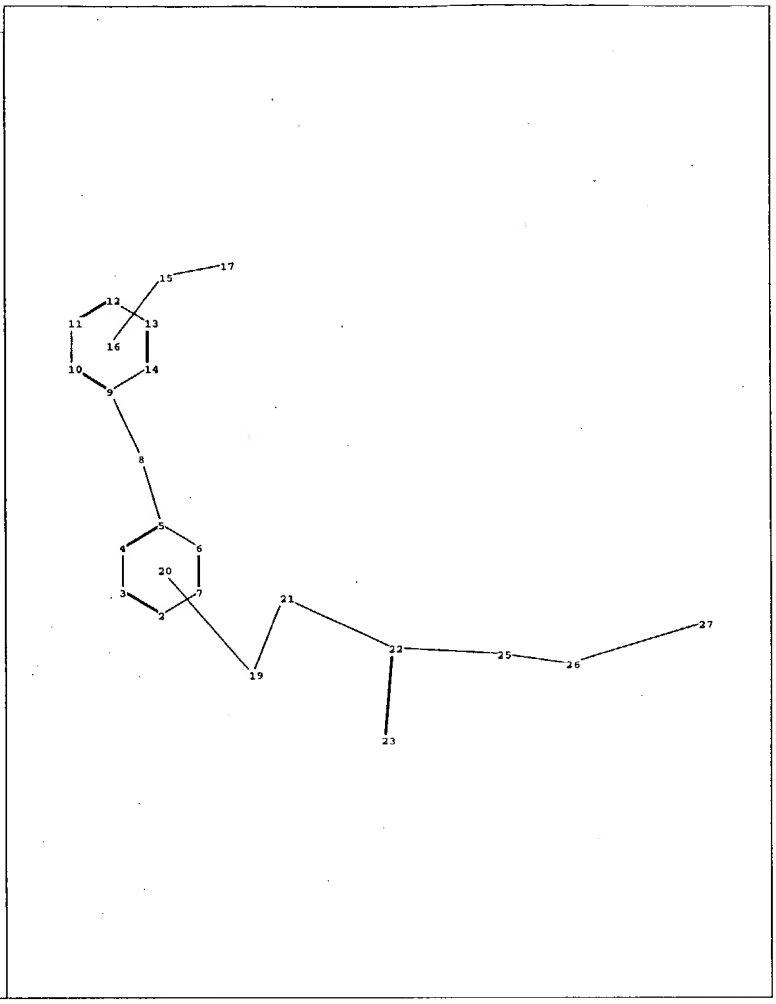
chain nodes :
2 9 11 13 14 15 16 18 19 20 21
ring nodes :
3 4 5 6 7 8
chain bonds :
2-3 2-21 9-11 13-14 13-21 14-15 15-16 15-18 18-19 19-20
ring bonds :
3-4 3-8 4-5 5-6 6-7 7-8
exact/norm bonds :
2-3 2-21 9-11 13-14 14-15 15-16 15-18 18-19 19-20
exact bonds :
13-21
normalized bonds :
3-4 3-8 4-5 5-6 6-7 7-8
isolated ring systems :
containing 3 :

G1:O,S

Match level :
2:CLASS 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:CLASS 10:CLASS 11:CLASS
13:CLASS 14:CLASS 15:CLASS 16:CLASS 18:CLASS 19:CLASS 20:Atom 21:Atom

C:\stnweb\Queries\89.str



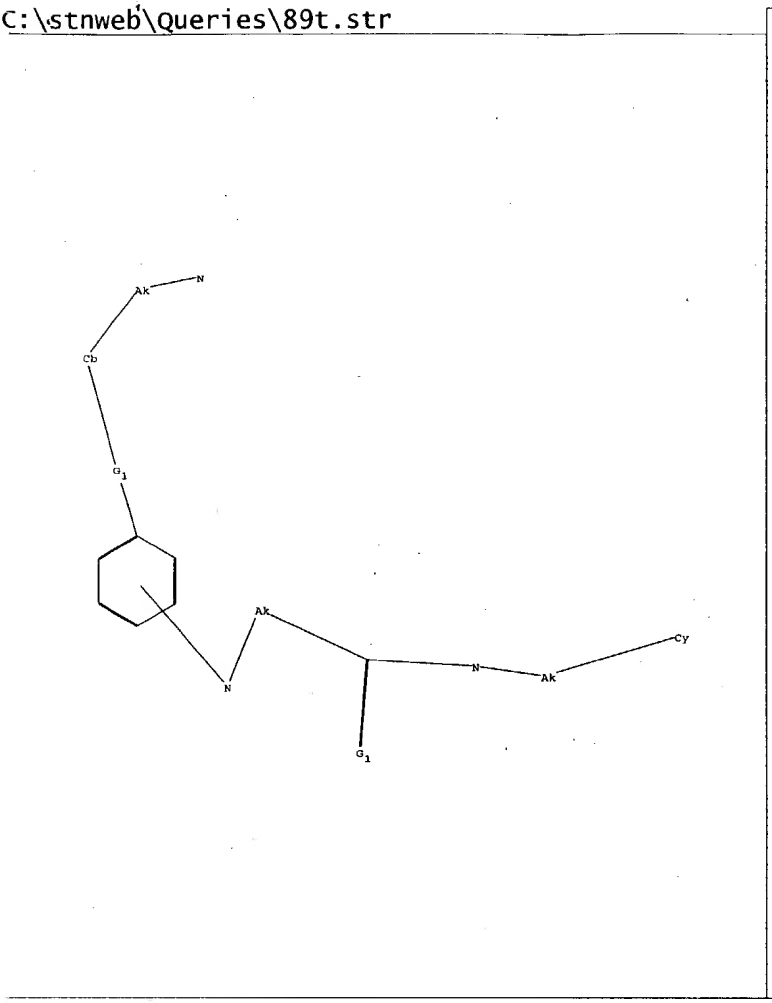


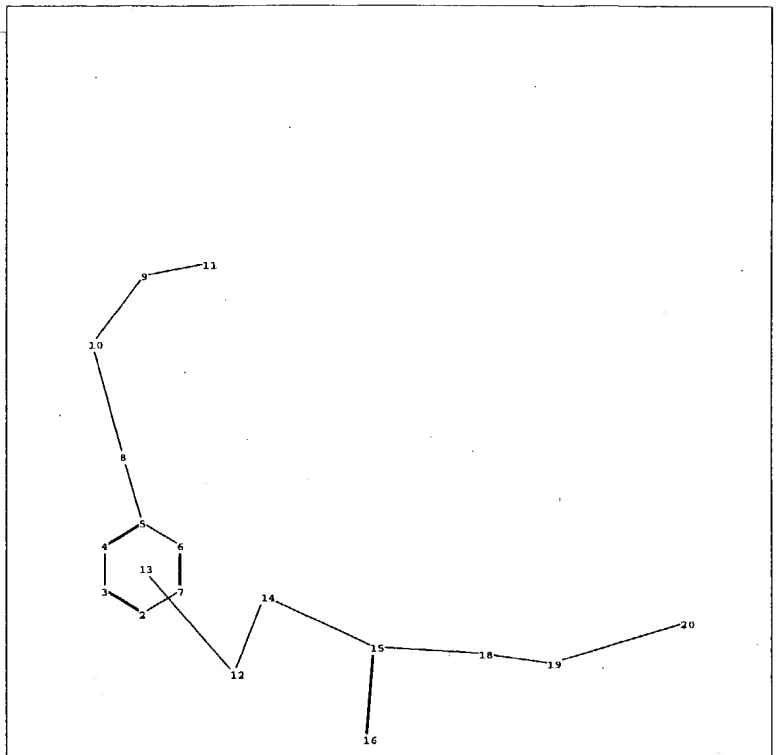
chain nodes :
8 15 17 19 21 22 23 25 26 27
ring nodes :
2 3 4 5 6 7 9 10 11 12 13 14
chain bonds :
5-8 8-9 15-17 19-21 21-22 22-23 22-25 25-26 26-27
ring bonds :
2-3 2-7 3-4 4-5 5-6 6-7 9-10 9-14 10-11 11-12 12-13 13-14
exact/norm bonds :
5-8 8-9 15-17 19-21 21-22 22-23 22-25 25-26 26-27
normalized bonds :
2-3 2-7 3-4 4-5 5-6 6-7 9-10 9-14 10-11 11-12 12-13 13-14
isolated ring systems :
containing 2 : 9 :

G1:O,S

Match level :
2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:CLASS 9:Atom 10:Atom 11:Atom 12:Atom
13:Atom 14:Atom 15:CLASS 16:CLASS 17:CLASS 19:CLASS 20:CLASS 21:CLASS 22:CLASS
23:CLASS 25:CLASS 26:CLASS 27:Atom

C:\stnweb\Queries\89t.str



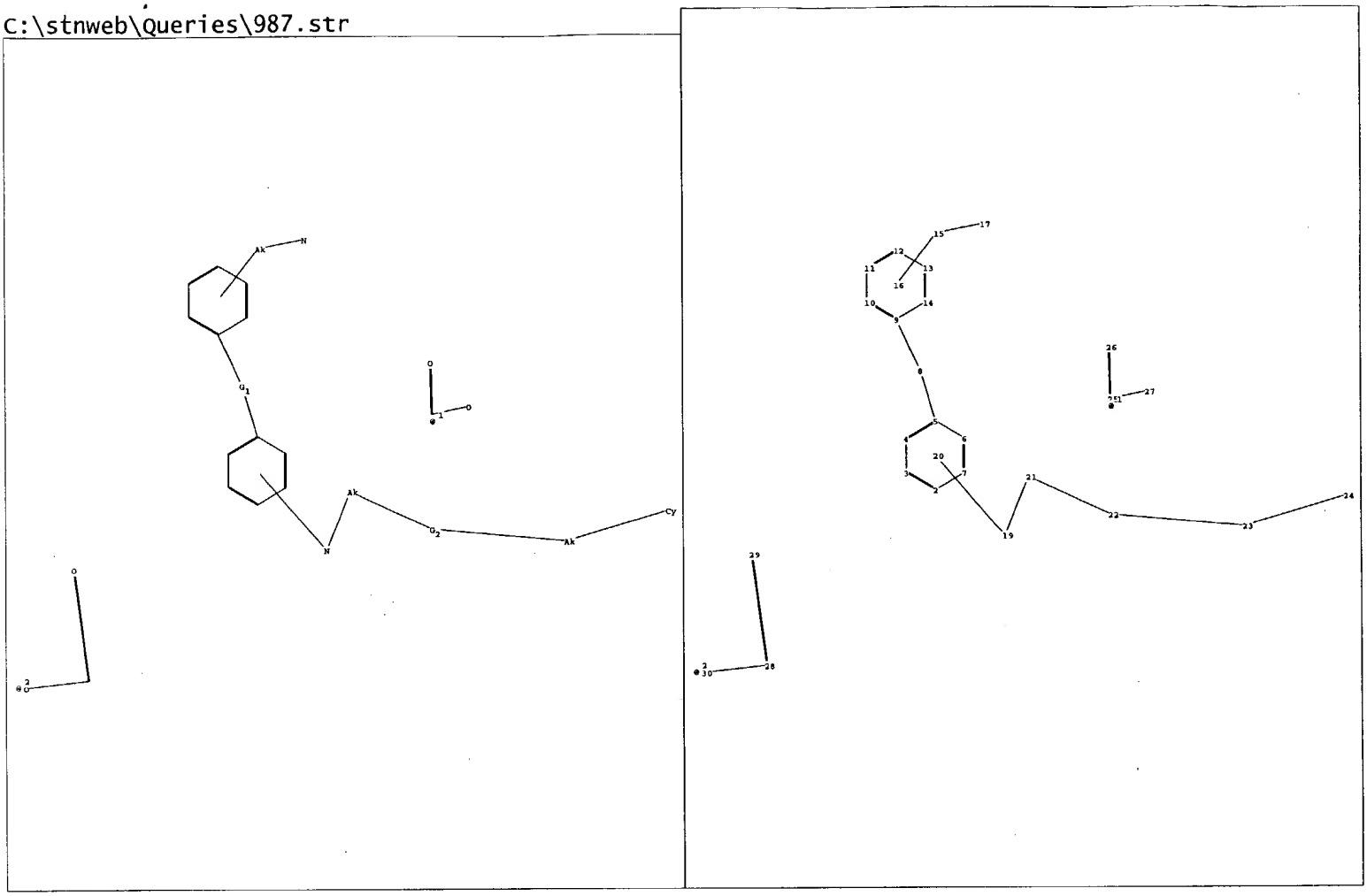


chain nodes :
8 9 10 11 12 14 15 16 18 19 20
ring nodes :
2 3 4 5 6 7
chain bonds :
5-8 8-10 9-10 9-11 12-14 14-15 15-16 15-18 18-19 19-20
ring bonds :
2-3 2-7 3-4 4-5 5-6 6-7
exact/norm bonds :
5-8 8-10 9-10 9-11 12-14 14-15 15-16 15-18 18-19 19-20
normalized bonds :
2-3 2-7 3-4 4-5 5-6 6-7

G1:O,S

Match level :
2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:CLASS 9:CLASS 10:CLASS 11:CLASS
12:CLASS 13:CLASS 14:CLASS 15:CLASS 16:CLASS 18:CLASS 19:CLASS 20:Atom

C:\stnweb\Queries\987.str



chain nodes :
8 15 17 19 21 22 23 24 25 26 27 28 29 30
ring nodes :
2 3 4 5 6 7 9 10 11 12 13 14
chain bonds :
5-8 8-9 15-17 19-21 21-22 22-23 23-24 25-26 25-27 28-29 28-30
ring bonds :
2-3 2-7 3-4 4-5 5-6 6-7 9-10 9-14 10-11 11-12 12-13 13-14
exact/norm bonds :
5-8 8-9 15-17 19-21 21-22 22-23 23-24 25-26 25-27 28-29 28-30
normalized bonds :
2-3 2-7 3-4 4-5 5-6 6-7 9-10 9-14 10-11 11-12 12-13 13-14
isolated ring systems :
containing 2 : 9 :

G1:O,S

G2:[*1],[*2]

Match level :
2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:CLASS 9:Atom 10:Atom 11:Atom 12:Atom
13:Atom 14:Atom 15:CLASS 16:CLASS 17:CLASS 19:CLASS 20:CLASS 21:CLASS 22:CLASS
23:CLASS 24:Atom 25:CLASS 26:CLASS 27:CLASS 28:CLASS 29:CLASS 30:CLASS